9/20/2004

ANSWER 1 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN

AB A series of 1-alkyl- and 1-alkenyl-2,9,10-trioxatricyclo[4.3.1.03,8]decane s, models for the core orthoester structural moiety of resiniferatoxin and synaptolepis factors, was prepared by a transetherification reaction of (±)-all-cis-cyclohexane-1,2,4-triol and tri-Me orthocarboxylates. The synthesis of the starting tri-Me orthocarboxylates is also given in detail.

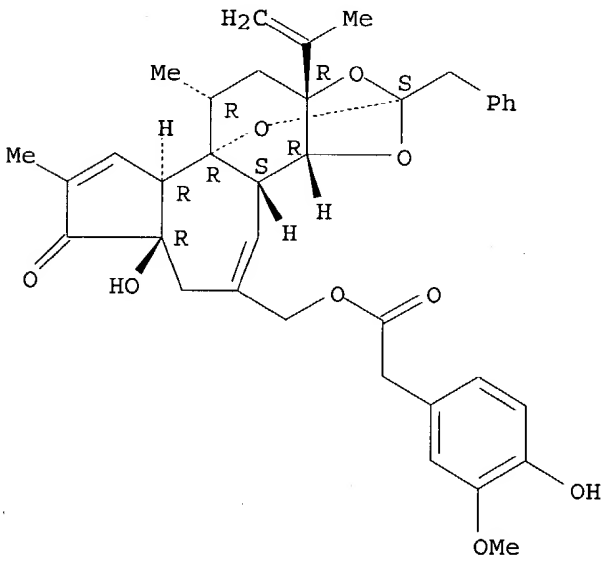
ACCESSION NUMBER: 2004:404883 CAPLUS
DOCUMENT NUMBER: 141:140628
TITLE: Synthesis of 1-substituted 2,9,10-trioxatricyclo[4.3.1.03,8]decanes
AUTHOR(S): Stanoeva, Elena; He, Weidong; Rocchetti, Maria Teresa; Nguyen Van, Tuyen; De Kimpe, Norbert
CORPORATE SOURCE: Faculty of Agricultural and Applied Biological Sciences, Department of Organic Chemistry, Ghent University, Ghent, B-9000, Belg.
SOURCE: Tetrahedron (2004), 60(23), 5077-5084
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:140628

IT **57444-62-9P**, Resiniferatoxin
RL: PNU (Preparation, unclassified); **PREP (Preparation)**
(preparation of trioxatricyclodecanes as orthoester core of resiniferatoxin and kirkinine)

RN 57444-62-9 CAPLUS

CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN

AB A mild protocol for the chemoselective deprotection of aryl methanesulfonates is described. The transformation is conducted on highly functionalized substrates and renders the methanesulfonate a useful, previously underutilized protecting group for phenols.

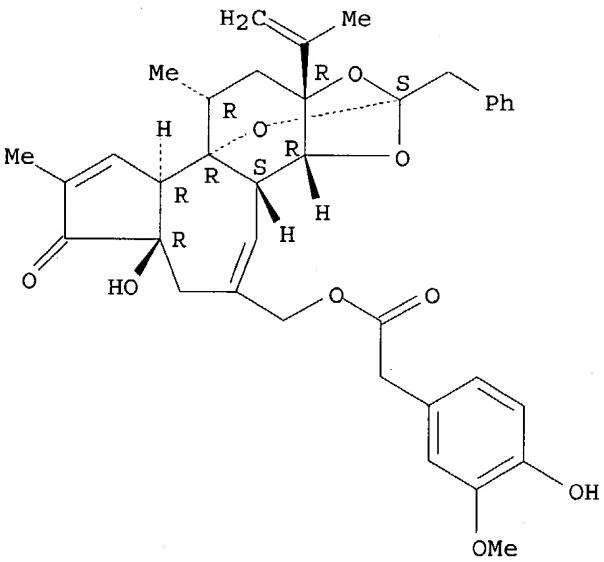
ACCESSION NUMBER: 2004:264146 CAPLUS
DOCUMENT NUMBER: 141:6885
TITLE: Mild cleavage of aryl mesylates. Methanesulfonate as potent protecting group for phenols
AUTHOR(S): Ritter, Tobias; Stanek, Kyrill; Larrosa, Igor; Carreira, Erick M.
CORPORATE SOURCE: Laboratorium fuer Organische Chemie, ETH Hoenggerberg, Zurich, CH-8093, Switz.
SOURCE: Organic Letters (2004), 6(9), 1513-1514
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:6885

IT **57444-62-9P**, Resiniferatoxin
RL: PNU (Preparation, unclassified); **PREP (Preparation)**
(cleavage reaction of aryl methanesulfonate protecting group of reactants used in the total synthesis of resiniferatoxin)

RN 57444-62-9 CAPLUS

CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

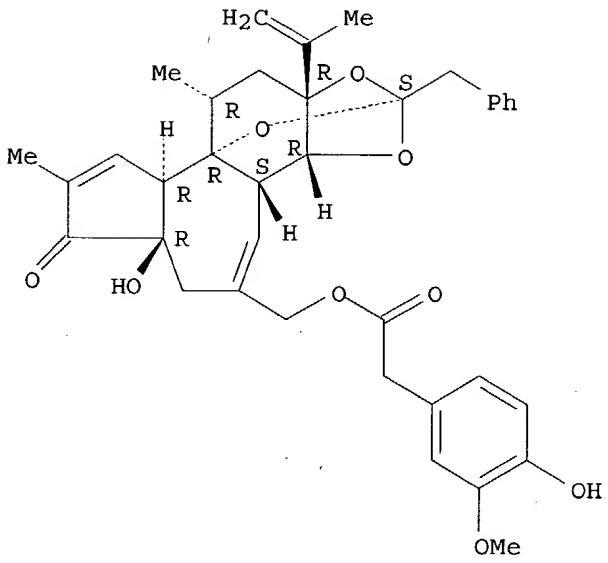
L4 ANSWER 3 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN

AB We previously described a series of N-(3-acyloxy-2-benzylpropyl) homovanillate and N'-(4-hydroxy-3-methoxybenzyl) thiourea derivs. that were potent VR1 agonists with high-affinities and excellent analgesic profiles. The design of these simplified RTX analogs was based on our RTX-derived pharmacophore model which incorporates the 4-hydroxy-3-methoxyphenyl (A-region), C20-ester (B-region), orthophenyl (C1-region) and C3-keto (C2-region) groups of RTX. For the purpose of optimizing the spatial arrangement of the four principal pharmacophores on the lead agonists (1-4), we have modified the distances in the parent C-region, 3-acyloxy-2-benzylpropyl groups, by lengthening or shortening one carbon to vary the distances between the pharmacophores. We find that two of the amides, 4 and 19, possess EC50 values <1 nM for induction of

calcium influx in the VR1-CHO cells. As observed previously, the structure-activity relations for inhibition of RTX binding to VR1 and for induction of calcium uptake were distinct, presumably reflecting both intrinsic and methodol. factors. In order to find the active conformation of VR1 ligands, the energy-minimized conformations of seven selected agonists were determined and the positions of their four pharmacophores were matched with those of five low energy RTX conformations. The rms values for the overlaps in the pharmacophores were calculated and correlated with the measured binding affinities (Ki) and calcium influx (EC50) values. The binding affinities of the agonists correlated best with the RMS values derived from RTX conformation E (r2=0.92), predicting a model of the active conformation of RTX and related vanilloids for binding to VR1. Poorer correlation was obtained between any of the conformations and the EC50 values for calcium influx.

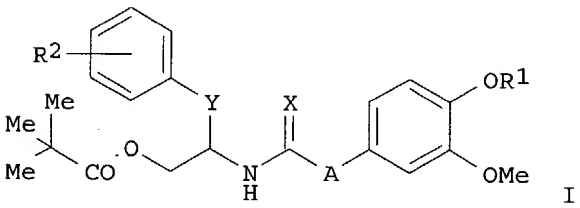
ACCESSION NUMBER: 2004:151250 CAPLUS
DOCUMENT NUMBER: 140:399330
TITLE: Structure-activity relationships of simplified resiniferatoxin analogues with potent VR1 agonism elucidates an active conformation of RTX for VR1 binding
AUTHOR(S): Lee, Jeewoo; Kim, Su Yeon; Park, Soyoung; Lim, Ju-Ok; Kim, Ji-Min; Kang, Myungshim; Lee, Jiyoun; Kang, Sang-Uk; Choi, Hyun-Kyung; Jin, Mi-Kyung; Welter, Jacqueline D.; Szabo, Tamas; Tran, Richard; Pearce, Larry V.; Toth, Attila; Blumberg, Peter M.
CORPORATE SOURCE: College of Pharmacy, Research Institute of Pharmaceutical Sciences, Laboratory of Medicinal Chemistry, Seoul National University, Shinlim-Dong, Kwanak-Ku, Seoul, 151-742, S. Korea
SOURCE: Bioorganic & Medicinal Chemistry (2004), 12(5), 1055-1069
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **57444-62-9DP**, Resiniferatoxin, analogs
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(structure-activity relationships of resiniferatoxin analogs with potent VR1 agonism reveals conformation of RTX for VR1 binding)
RN 57444-62-9 CAPLUS
CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
GI



I

AB Vanilloid analogs, such as I [R1 = H, (CH2)2NH2, alkoxyalkyl; R2 = H, halogen alkyl; A = -NHCH2-, -CH2NH-, -CH2-, etc.; X = O, S; Y = -(CH2)n-; n = 1-3] containing resiniferatoxin pharmacophores, were prepared for use in pharmaceutical compns. as vanilloid receptor agonists and potent analgesics. These pharmaceutical compns. are useful for preventing, alleviating or treating pain, acute pain, chronic pain, neuropathic pain, post-operative pain, migraine, arthralgia, neutopathies, nerve injury, diabetic neuropathy, neurodegeneration, neurotic skin disorder, stroke, urinary bladder hypersensitiveness, irritable bowel syndrome, a respiratory disorder such as asthma or chronic obstructive pulmonary disease, irritation of skin, eye or mucous membrane, fervescence, stomach-duodenal ulcer, inflammatory bowel disease, inflammatory disease or urgent urinary incontinence. Thus, I [R1 = H, R2 = 3,4-Me2, A = -NHCH2-, X = S, Y = -(CH2)2-] was prepared via reaction of the corresponding amine, 3,4-Me2C6H3(CH2)2CH(CH2NH2)CH2OCOCMe3, with an O-protected-4-(isothiocyanatomethyl)-2-methoxyphenol. The prepared vanilloids were assayed for their effecton on vanilloid receptors and for a variety of other biol. activities.

ACCESSION NUMBER: 2003:261805 CAPLUS
DOCUMENT NUMBER: 138:271389
TITLE: Simplified resiniferatoxin analogs as vanilloid receptor agonist showing excellent analgesic activity and the pharmaceutical compositions containing the same
INVENTOR(S): Lee, Jee-Woo

PATENT ASSIGNEE(S): Digital Biotech Co., Ltd., S. Korea
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003027064	A1	20030403	WO 2002-KR1746	20020918
WO 2003027064	B1	20040408		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004063786	A1	20040401	US 2002-324393	20021218
PRIORITY APPLN. INFO.:			KR 2001-60028 A	20010927
			KR 2002-56280 A	20020916
			WO 2002-KR1746 A1	20020918

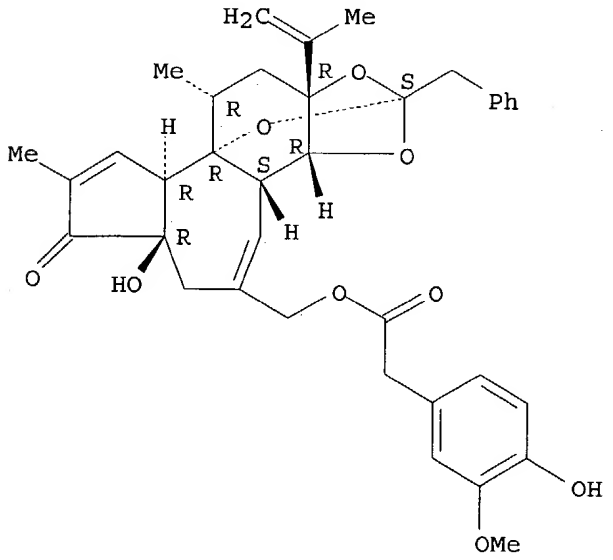
OTHER SOURCE(S): MARPAT 138:271389

IT **57444-62-9DP**, Resiniferatoxin, analogs
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation and formulation of simplified resiniferatoxin analogs as vanilloid receptor agonist showing excellent analgesic activity)

RN 57444-62-9 CAPLUS

CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN

AB The authors have synthesized iodinated resiniferatoxin bearing a 4-hydroxy-5-iodo-3-methoxyphenylacetate ester (I-RTX) and have characterized its activity on rat and human TRPV1 (VR1) receptors, as well as in behavioral assays of nociception. In whole cell patch-clamp recordings from transfected cells the functional activity of I-RTX was determined Currents activated by capsaicin exhibited characteristic outward rectification and were antagonized by capsazepine and I-RTX. On rat TRPV1 the affinity of I-RTX was 800-fold higher than that of capsazepine (IC50 = 0.7 and 562 nM, resp.) and 10-fold higher on rat vs. human receptors (IC50 = 0.7 and 5.4 nM, resp.). The same difference was observed when comparing the inhibition of [3H]RTX binding to rat and human TRPV1 membranes for both RTX and I-RTX. Addnl. pharmacol. differences were revealed using protons as the stimulus. Under these conditions capsazepine only partly blocked currents through rat TRPV1 receptors (by 70 to 80% block), yet was a full antagonist on human receptors. In contrast, I-RTX completely blocked proton-induced currents in both species and that activated by noxious heat. I-RTX also blocked capsaicin-induced firing of C-fibers in a rat in vitro skin-nerve assay. Despite this activity and the high affinity of I-RTX for rat TRPV1, only capsazepine proved to be an effective antagonist of capsaicin-induced paw flinching in rats. Thus, although I-RTX has limited utility for in vivo behavioral studies it is a high-affinity TRPV1 receptor antagonist that will be useful to characterize the functional properties of cloned and native vanilloid receptor subtypes in vitro.

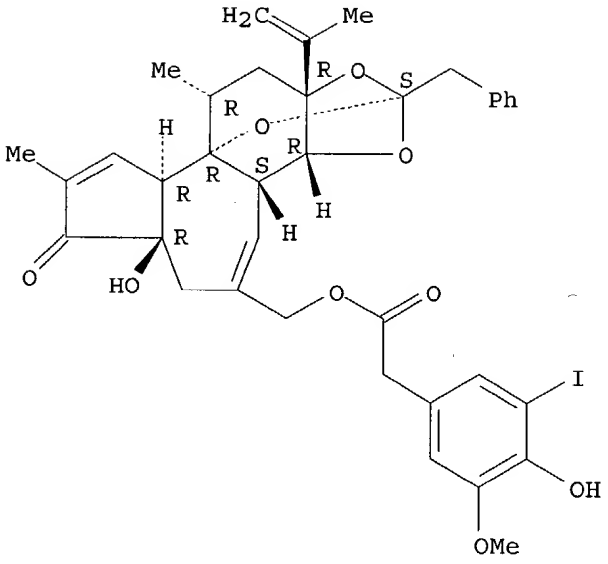
ACCESSION NUMBER: 2002:932569 CAPLUS
DOCUMENT NUMBER: 139:858
TITLE: Functional properties of the high-affinity TRPV1 (VR1) vanilloid receptor antagonist (4-hydroxy-5-iodo-3-methoxyphenylacetate ester) iodo-resiniferatoxin
AUTHOR(S): Seabrook, Guy R.; Sutton, Kathy G.; Jarolimek, Wolfgang; Hollingworth, Gregory J.; Teague, Simon; Webb, Janine; Clark, Natalie; Boyce, Susan; Kerby, Julie; Ali, Zahid; Chou, Margaret; Middleton, Richard; Kaczorowski, Gregory; Jones, A. Brian
CORPORATE SOURCE: The Neuroscience Research Centre, Merck Sharp and Dohme, Essex, UK
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2002), 303(3), 1052-1060
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **535974-91-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(functional properties of high-affinity TRPV1 (VR1) vanilloid receptor antagonist (4-hydroxyiodomethoxyphenylacetate ester) iodo-resiniferatoxin)

RN 535974-91-5 CAPLUS

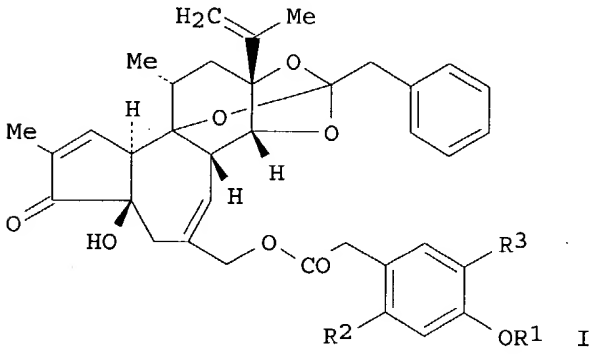
CN Benzeneacetic acid, 4-hydroxy-3-iodo-5-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
GI



AB Resiniferatoxin derivs., such as I [R1 = H, CHO, acyl; R2 = iodo, 125I, 131I; R3 = OH, alkoxy], were prepared for use as ligands in vanilloid receptor binding assays. Thus, resiniferatoxin derivative I (R1 = COMe,R2 = iodo, R3 = OMe) was prepared in 59% yield by esterification of resiniferonol 9,13,14-orthophenylacetate with 4-acetyloxy-2-iodo-5-methoxybenzeneacetic acid using dicyclohexylcarbodiimide and 4-(dimethylamino)pyridine in CH2Cl2. The acetate was then converted to the corresponding phenol I (R1 = H, R2 = iodo, R3 = OMe) with 68% yield using pyrrolidine in CH2Cl2. I (R1 = COMe,R2 = iodo, R3 = OMe) and I (R1 = H, R2 = iodo, R3 = OMe) gave IC50 values of 0.31 ± 0.06 and 0.22 ± 0.03, resp., when assayed human VR1 receptor binding affinity.

ACCESSION NUMBER: 2002:293659 CAPLUS
DOCUMENT NUMBER: 136:325707
TITLE: Preparation of labeled resiniferatoxin derivatives for use as radioligands in vanilloid receptor binding assays
INVENTOR(S): McDonnell, Mark E.; Weaner, Larry E.; Zhang, Sui-Po
PATENT ASSIGNEE(S): Ortho-Mcneil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030937	A2	20020418	WO 2001-US42548	20011009
WO 2002030937	A3	20030206		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002019783	A5	20020422	AU 2002-19783	20011009
EP 1341795	A2	20030910	EP 2001-986690	20011009
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004511488	T2	20040415	JP 2002-534323	20011009
PRIORITY APPLN. INFO.:			US 2000-239627P P	20001010
			WO 2001-US42548 W	20011009

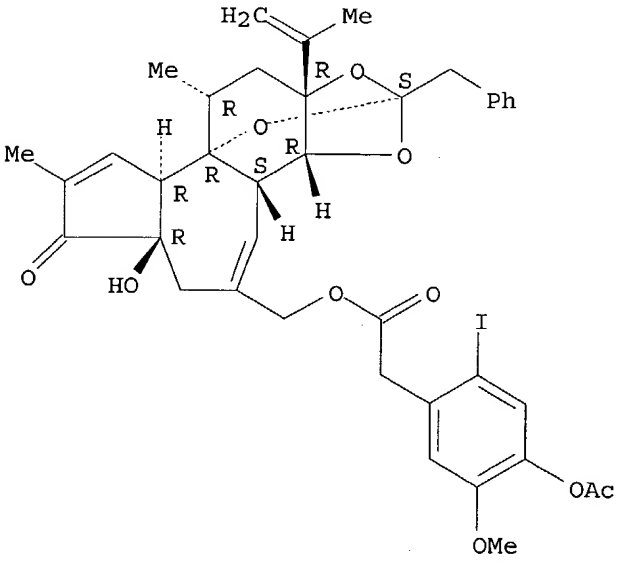
OTHER SOURCE(S): MARPAT 136:325707

IT **412271-86-4P**
RL: DGN (Diagnostic use); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation of labeled resiniferatoxin derivs. for use as radioligands in vanilloid receptor binding assays)

RN 412271-86-4 CAPLUS

CN Benzeneacetic acid, 4-(acetyloxy)-2-iodo-5-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

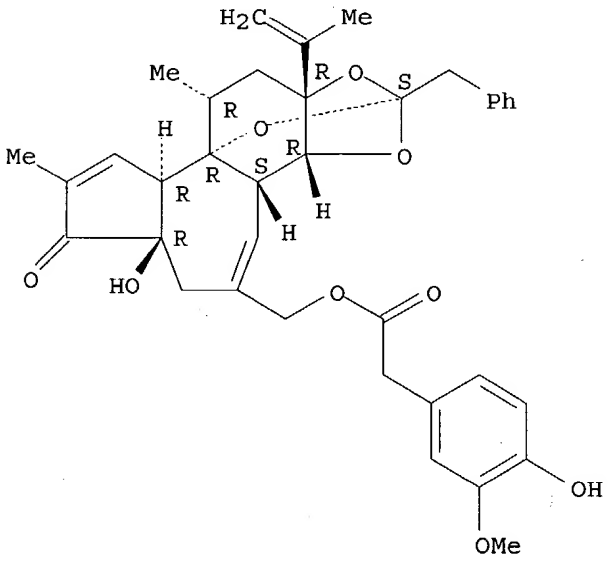


IT **57444-62-9DP**, Resiniferatoxin, derivs. **412271-87-5P**

412271-88-6P 412271-89-7P 412271-90-0P
412271-91-1P
RL: DGN (Diagnostic use); PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of labeled resiniferatoxin derivs. for use as radioligands in vanilloid receptor binding assays)

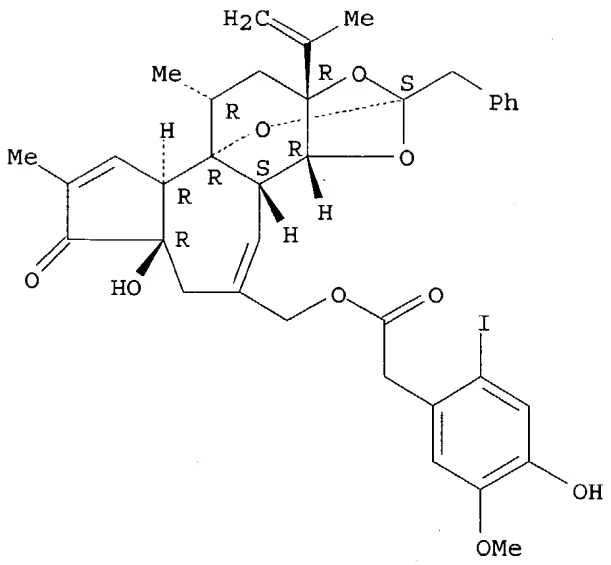
RN 57444-62-9 CAPLUS
CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



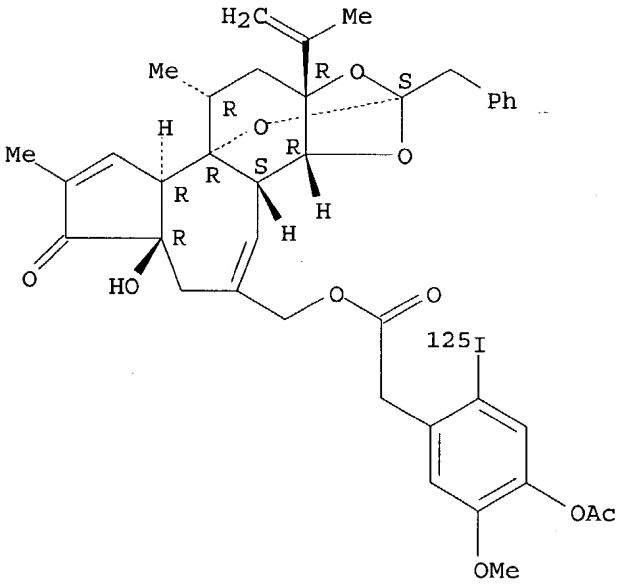
RN 412271-87-5 CAPLUS
CN Benzeneacetic acid, 4-hydroxy-2-iodo-5-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



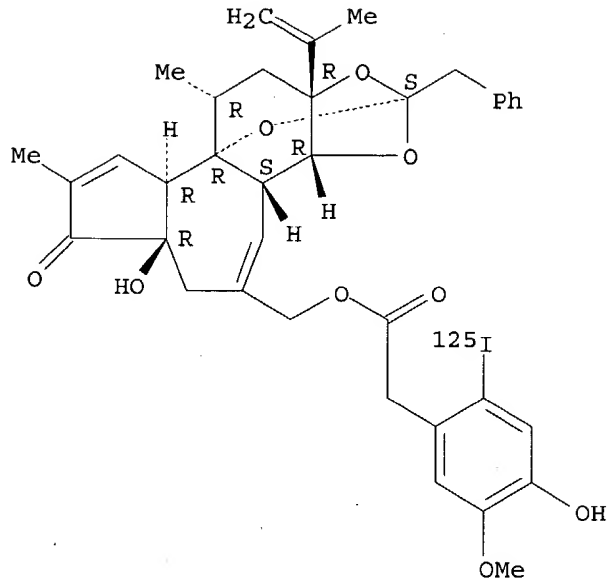
RN 412271-88-6 CAPLUS
CN Benzeneacetic acid, 4-(acetyloxy)-2-(iodo-125I)-5-methoxy-, [(2S,3aR,3bR,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 412271-89-7 CAPLUS
CN Benzeneacetic acid, 4-hydroxy-2-(iodo-125I)-5-methoxy-, [(2S,3aR,3bR,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

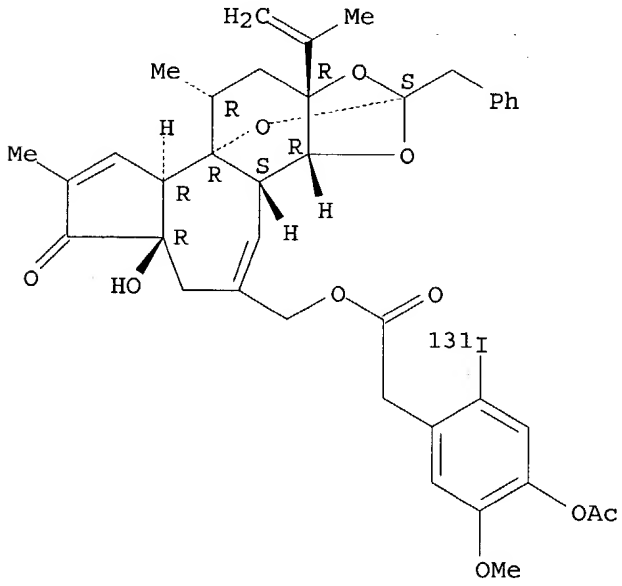
Absolute stereochemistry.



RN 412271-90-0 CAPLUS

CN Benzeneacetic acid, 4-(acetyloxy)-2-(iodo-131I)-5-methoxy-, [(2S,3aR,3bR,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

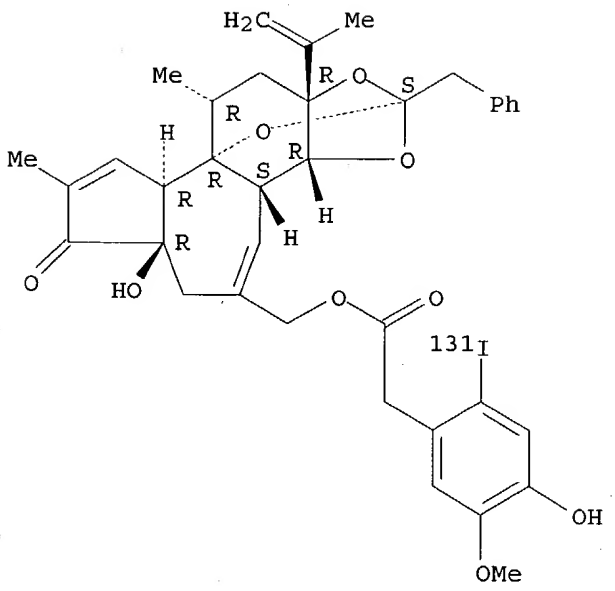
Absolute stereochemistry.



RN 412271-91-1 CAPLUS

CN Benzeneacetic acid, 4-hydroxy-2-(iodo-131I)-5-methoxy-, [(2S,3aR,3bR,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 7 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN

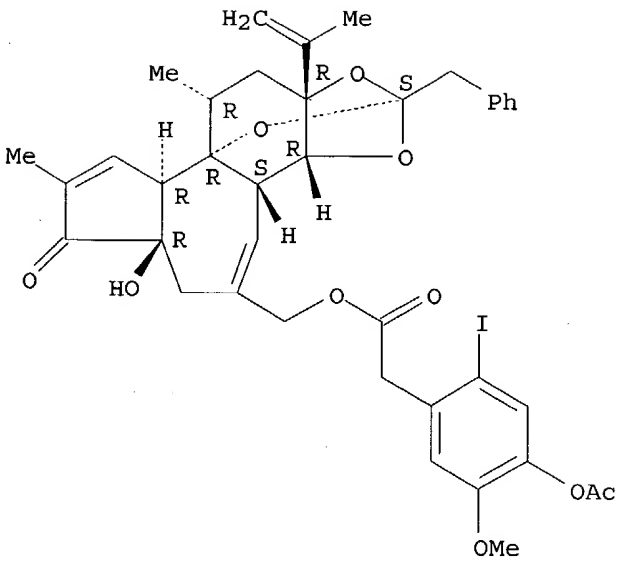
AB Using a 'directed' iodination procedure, novel iodo-resiniferatoxin congeners were synthesized from 4-acetoxy-3-methoxyphenylacetic acid and resiniferinol- 9,13,14-ortho-phenylacetate (ROPA). The 2-iodo-4-hydroxy-5-methoxyphenylacetic acid ester of resiniferinol displayed high affinity binding (Ki=0.71 nM) for the human vanilloid VR1 receptor and functioned as a partial agonist.

ACCESSION NUMBER: 2002:251346 CAPLUS
DOCUMENT NUMBER: 137:125294
TITLE: Synthesis and in vitro evaluation of a novel iodinated resiniferatoxin derivative that is an agonist at the human vanilloid VR1 receptor
AUTHOR(S): McDonnell, Mark E.; Zhang, Sui-Po; Dubin, Adrienne E.; Dax, Scott L.
CORPORATE SOURCE: Johnson & Johnson Pharmaceutical Research and Development, Spring House, PA, 19477, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(8), 1189-1192
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:125294

IT **412271-86-4P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent)
(synthesis of a novel iodinated resiniferatoxin derivative via a directed iodination procedure and evaluation as an agonist at the human vanilloid VR1 receptor)

RN 412271-86-4 CAPLUS
CN Benzeneacetic acid, 4-(acetyloxy)-2-iodo-5-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

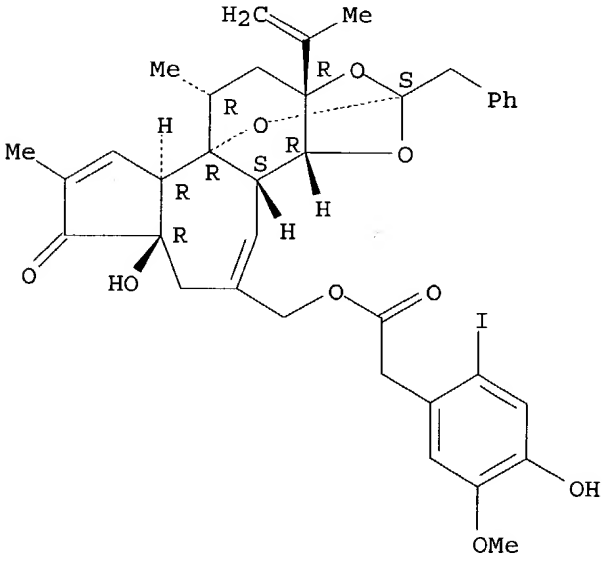


IT **412271-87-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**
(synthesis of a novel iodinated resiniferatoxin derivative via a directed iodination procedure and evaluation as an agonist at the human vanilloid VR1 receptor)

RN 412271-87-5 CAPLUS

CN Benzeneacetic acid, 4-hydroxy-2-iodo-5-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

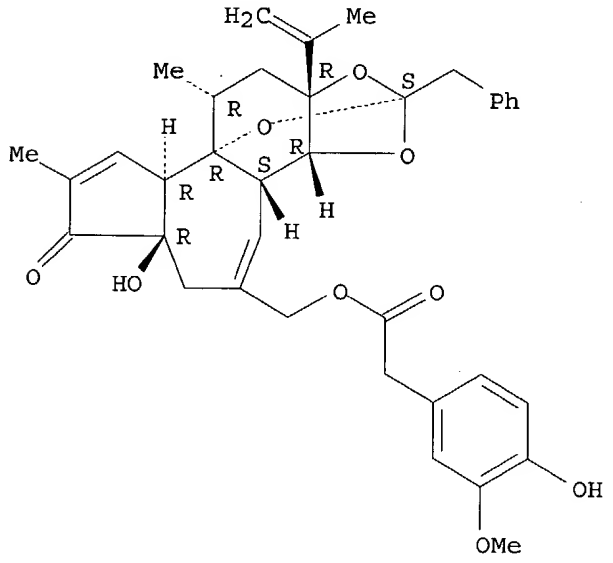
Absolute stereochemistry.



IT **57444-62-9DP**, Resiniferatoxin, analogs
RL: PNU (Preparation, unclassified); **PREP (Preparation)**
(synthesis of a novel iodinated resiniferatoxin derivative via a directed iodination procedure and evaluation as an agonist at the human vanilloid VR1 receptor)

RN 57444-62-9 CAPLUS
CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
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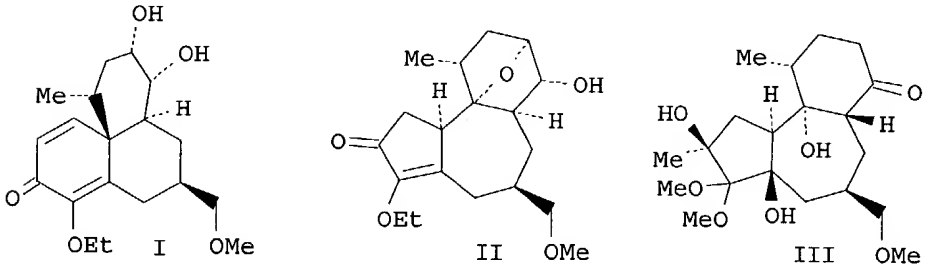
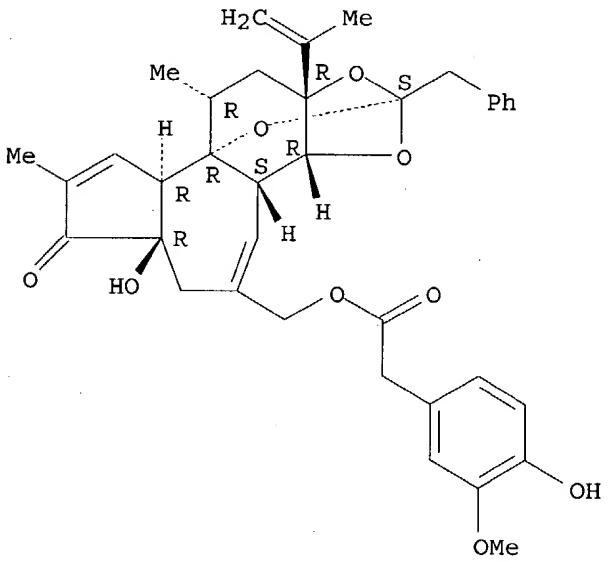


AB The utility of a 2,5-cyclohexadienone (I) photorearrangement within a complex tricyclic system to a 5,7,6-tricyclic structure (II) for the formation of a highly functionalized template structure (III) for the daphnanes and (+)-resiniferatoxin was described.

ACCESSION NUMBER: 2001:553424 CAPLUS
DOCUMENT NUMBER: 135:318594
TITLE: Rearrangement of a tricyclic 2,5-cyclohexadienone: Towards a general synthetic route to the daphnanes and (+)-resiniferatoxin
AUTHOR(S): Jackson, Stona R.; Johnson, Michael G.; Mikami, Masafumi; Shiokawa, Sojiro; Carreira, Erick M.
CORPORATE SOURCE: Lab. Organische Chemie, ETH-Zentrum, Zurich, 8092, Switz.
SOURCE: Angewandte Chemie, International Edition (2001), 40(14), 2694-2697

CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:318594
IT **57444-62-9P**, (+)-Resiniferatoxin
RL: PNU (Preparation, unclassified); **PREP (Preparation)**
(formal synthesis of daphnanes via photorearrangement of a tricyclic cyclohexadienone)
RN 57444-62-9 CAPLUS
CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

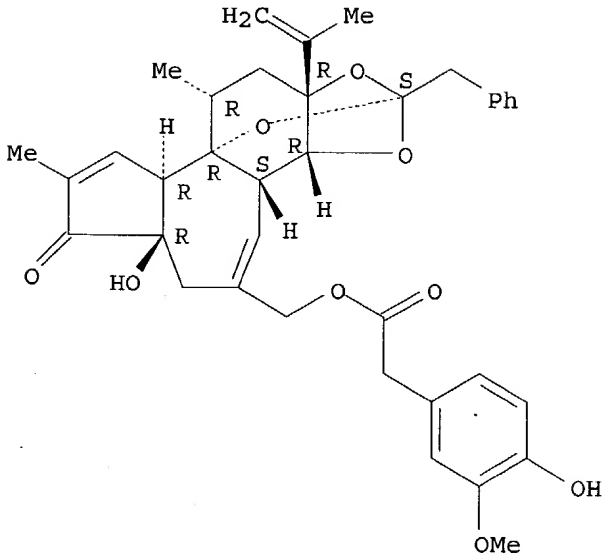
Absolute stereochemistry.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
AB Unavailable
ACCESSION NUMBER: 2000:571059 CAPLUS
DOCUMENT NUMBER: 134:115690
TITLE: Photorearrangement of tricyclic 2,5-cyclohexadienones in a synthetic route toward the natural product resiniferatoxin
AUTHOR(S): Johnson, Michael Garrett
CORPORATE SOURCE: California Institute of Technology, USA
SOURCE: (2000) 224 pp. Avail.: UMI, Order No. DA9956112
From: Diss. Abstr. Int., B 2000, 60(12), 6108
DOCUMENT TYPE: Dissertation
LANGUAGE: English
IT **57444-62-9P**, Resiniferatoxin
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(photorearrangement of tricyclic 2,5-cyclohexadienones in synthetic route toward the natural product resiniferatoxin)
RN 57444-62-9 CAPLUS
CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 10 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
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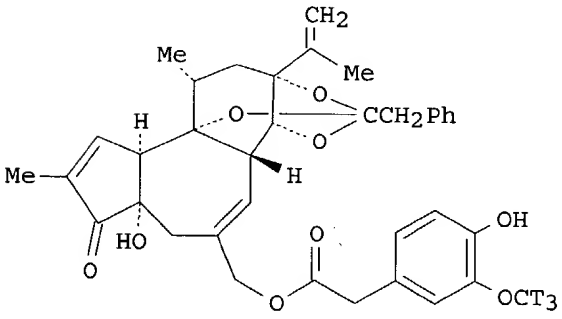


I

AB Tritiated resiniferatoxin (I) with three tritium atoms per mol. was prepared by a one-step procedure: methylation of its desmethyl derivative with carrier-free C3H3I, followed by separation of the resulting 1:1 regioisomeric mixture by semi-preparative reverse-phase HPLC. The desmethyl resiniferatoxin precursor was obtained from coupling of (3,4-dihydroxyphenyl)acetic acid to resiniferonol-9,13,14-orthophenylacetate.

ACCESSION NUMBER: 2000:550046 CAPLUS
DOCUMENT NUMBER: 133:310018
TITLE: Synthesis of tritiated resiniferatoxin
AUTHOR(S): Shu, Arthur Y. L.; Heys, J. Richard
CORPORATE SOURCE: Radiochemistry Section, Department of Synthetic Chemistry, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406, USA
SOURCE: Synthesis and Applications of Isotopically Labelled Compounds 1997, Proceedings of the International Symposium, 6th, Philadelphia, PA, United States, Sept.

14-18, 1997 (1998), Meeting Date 1997, 463-466.
Editor(s): Heys, J. Richard; Melillo, David G. John Wiley & Sons Ltd.: Chichester, UK.
CODEN: 69AGFQ

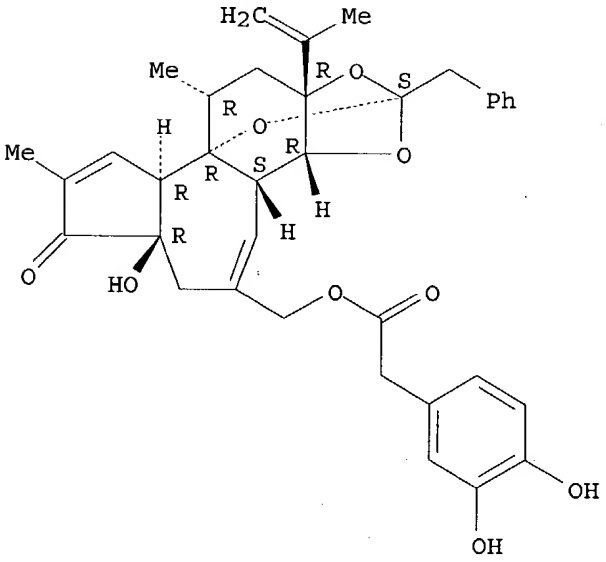
DOCUMENT TYPE: Conference
LANGUAGE: English

IT **301843-07-2P**, Desmethylresiniferatoxin
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(synthesis of tritiated resiniferatoxin via methylation with radioactive Me iodide)

RN 301843-07-2 CAPLUS

CN Benzeneacetic acid, 3,4-dihydroxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

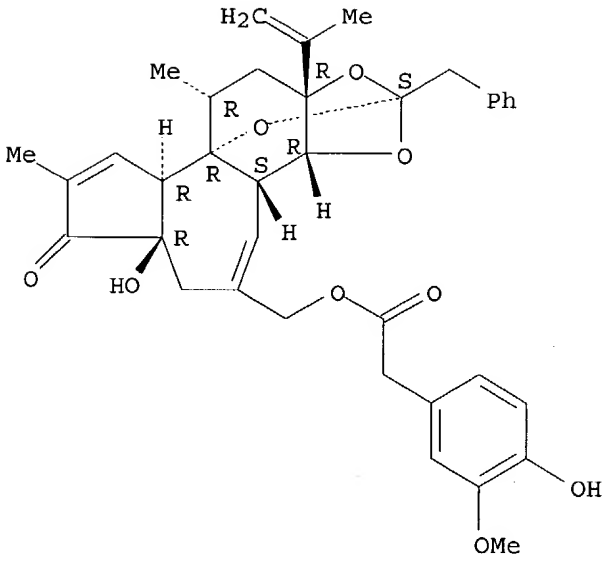


IT **57444-62-9DP**, Resiniferatoxin, tritiated **83117-38-8P**, Resiniferatoxin 4''-methyl ether **301670-35-9P** **301670-36-0P** **301843-09-4P**, 4''-O-Methyldesmethylresiniferatoxin
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(synthesis of tritiated resiniferatoxin via methylation with radioactive Me iodide)

RN 57444-62-9 CAPLUS

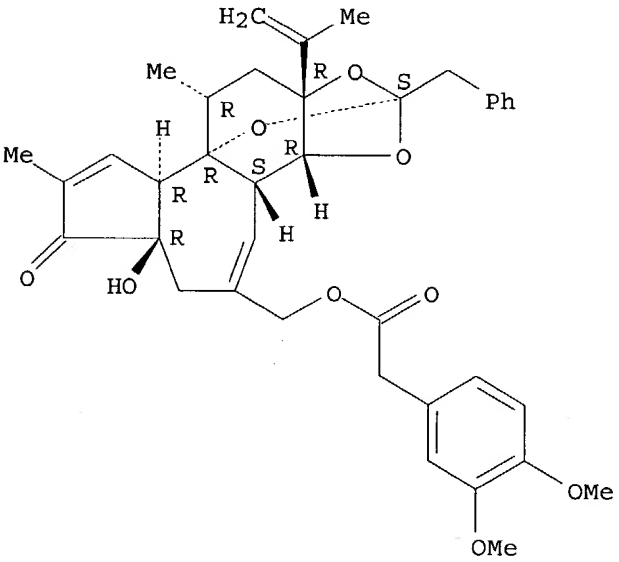
CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



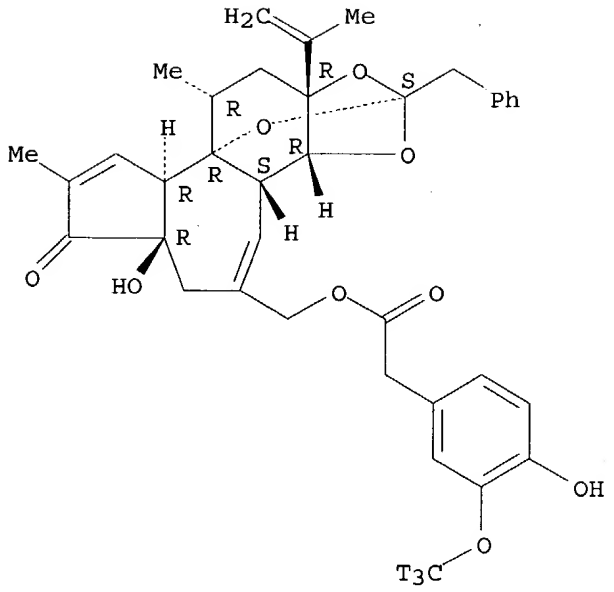
RN 83117-38-8 CAPLUS
CN Benzeneacetic acid, 3,4-dimethoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



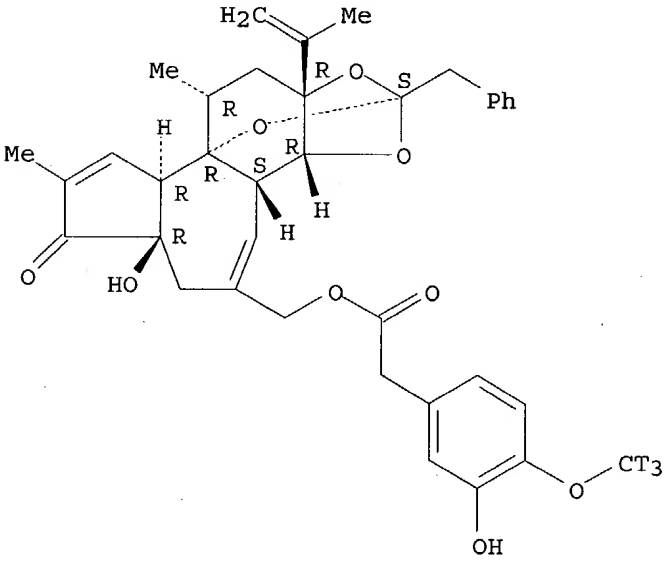
RN 301670-35-9 CAPLUS
CN Benzeneacetic acid, 4-hydroxy-3-(methoxy-t3)-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



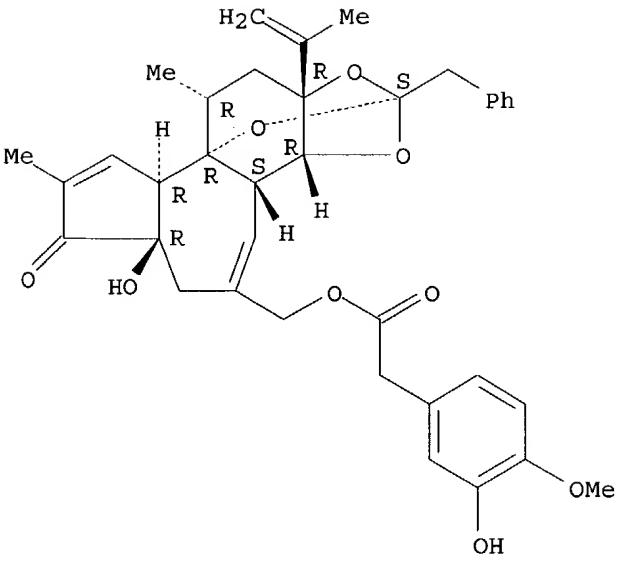
RN 301670-36-0 CAPLUS
CN Benzeneacetic acid, 3-hydroxy-4-(methoxy-t3)-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 301843-09-4 CAPLUS
CN Benzeneacetic acid, 3-hydroxy-4-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN

AB The title research of P. A. Wender, C. D. Jesudason, H. Nakahira, N. Tamura, A. L. Tebbe, and Y. Ueno (1997) is reviewed with commentary and 6 refs.

ACCESSION NUMBER: 1998:566967 CAPLUS

DOCUMENT NUMBER: 129:276024

TITLE: The first synthesis of a daphnane diterpene: the enantiocontrolled total synthesis of (+)-resiniferatoxin

AUTHOR(S): Boger, Dale L.; Searcey, Mark

CORPORATE SOURCE: The Scripps Research Institute, USA

SOURCE: Chemtracts (1998), 11(9), 647-651
CODEN: CHEMFW; ISSN: 1431-9268

PUBLISHER: Springer-Verlag New York Inc.

DOCUMENT TYPE: Journal; General Review

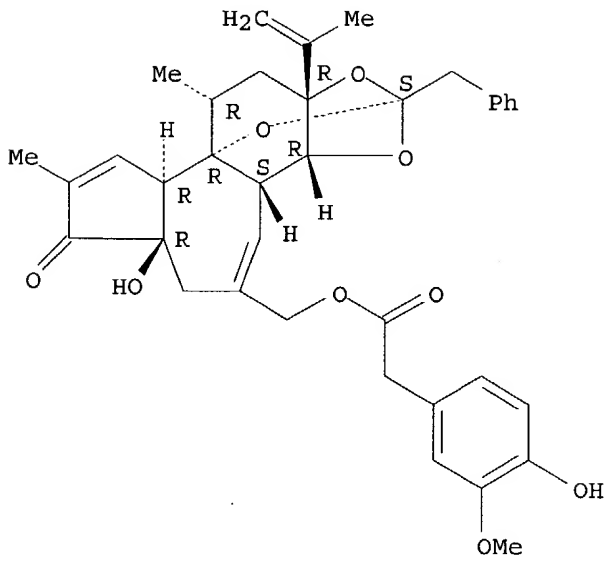
LANGUAGE: English

IT **57444-62-9P**, (+)-Resiniferatoxin
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(enantiocontrolled total synthesis of (+)-resiniferatoxin)

RN 57444-62-9 CAPLUS

CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN

AB A review with 35 refs. on paclitaxel and resiniferatoxin (RTX), diterpenoids with a unique mechanism of activity and great pharmacol. potential. Two series of novel paclitaxel analogs (C-secotaxols and pyrazolinetaxols) were prepared exploiting the nucleophilic and reductive trapping of the C-seco aldehydic tautomer of taxanes of the 10-deacetyl-10-dehydrobaccatin III-type. As an example of utilisation of alkaloidal left-overs from yew biomass, the synthesis of azetidine isosteres of oxetane-type taxoids is presented. Finally, the design and synthesis of the phorbol-RTX hybrid PPAHV (phorbol-12-phenylacetate-13-acetate-20-homovanillate) is described. This compound displayed a unique pattern of vanilloid activity, whose relevance is discussed.

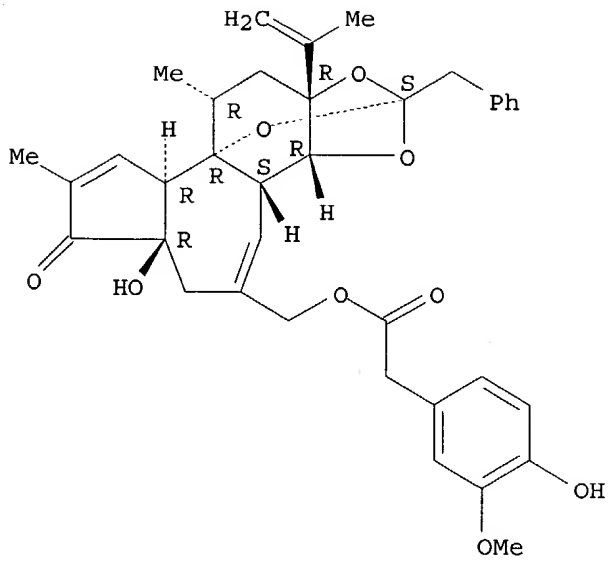
ACCESSION NUMBER: 1998:131048 CAPLUS
DOCUMENT NUMBER: 128:217508
TITLE: Biologically active diterpenoids. Synthesis of analogs of paclitaxel and resiniferatoxin
AUTHOR(S): Appendino, Giovanni
CORPORATE SOURCE: Dipartimento di Scienza e Tecnologia del Farmaco, Universita di Torino, Turin, I-10125, Italy
SOURCE: Gazzetta Chimica Italiana (1997), 127(8), 461-469
CODEN: GCITA9; ISSN: 0016-5603
PUBLISHER: Societa Chimica Italiana
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

IT **57444-62-9P**, Resiniferatoxin
RL: BUU (Biological use, unclassified); PNU (Preparation, unclassified); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(Synthesis of analogs of paclitaxel and resiniferatoxin, biol. active diterpenoids)

RN 57444-62-9 CAPLUS

CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Resiniferatoxin (I) is a daphnane diterpene, identified in the latex of Euphorbia resinifera on the basis of its extraordinary irritant activity. It is an ultrapotent capsaicin analog and has attracted special therapeutic interest as an analgesic agent, particularly for the treatment of pain associated with diabetic polyneuropathy and postherpetic neuralgia. I is also a key mol. probe for the investigation of the relatively little studied vanilloid receptor(s) and its biochem. This manuscript describes the first asym. synthesis of I, which marks the first synthesis of a daphnane as well. Absolute stereochem. is set in the first step of this synthesis through the asym. epoxidn. of divinyl carbinol. The daphnane BC-ring system and relative stereochem. at C8 and C9 are then established through one of the most complex versions of an intramol. oxidopyrylium cycloaddn. (pyranone II to tricycle III) reported thus far. The oxygen bridge produced in this process is used to protect the C9 hydroxyl group and to conformationally and facially bias the otherwise flexible B-ring, thereby allowing for control of stereogenesis at C4 and C10. The A-ring is then introduced through a sequence (III to daphnane IV) ultimately involving a complex but highly efficient zirconocene mediated ene-yne cyclization. The relatively uncommon orthoester functionality and the C20 homovanillyl chain are then introduced toward the end of the synthesis in order to minimize handling of potentially active intermediates and to maximize flexibility with respect to analog preparation This flexible entry into the daphnane family provides the basis for structure-activity, receptor characterization, and mode of action studies which have thus far been restricted by the complexity, potency, and limited availability of daphnanes and their analogs.

ACCESSION NUMBER: 1998:48047 CAPLUS
DOCUMENT NUMBER: 128:61644
TITLE: The First Synthesis of a Daphnane Diterpene: The Enantiocontrolled Total Synthesis of (+)-Resiniferatoxin

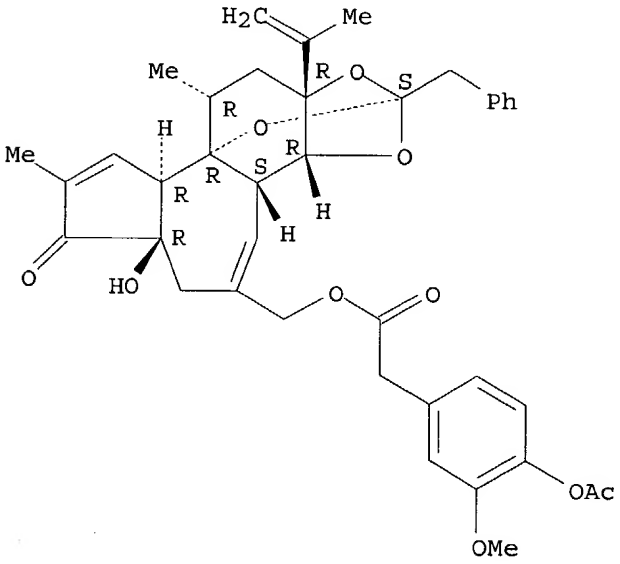
AUTHOR(S): Wender, Paul A.; Jesudason, Cynthia D.; Nakahira, Hiroyuki; Tamura, Norikazu; Tebbe, Anne Louise; Ueno, Yoshihide
CORPORATE SOURCE: Department of Chemistry, Stanford University, Stanford, CA, 94305, USA
SOURCE: Journal of the American Chemical Society (1997), 119(52), 12976-12977
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 128:61644

IT **71407-32-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(enantiocontrolled total synthesis of resiniferatoxin via an intramol. oxidopyrylium cycloaddn.)

RN 71407-32-4 CAPLUS

CN Benzeneacetic acid, 4-(acetyloxy)-3-methoxy-, [3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester, [2S-(2α,3aβ,3bβ,6aβ,9aα,9bα,10.alpha.,11aβ)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

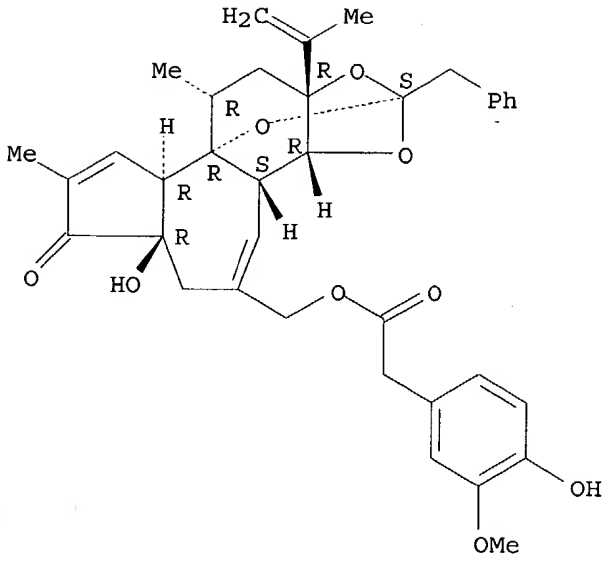


IT **57444-62-9P**, (+)-Resiniferatoxin
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(enantiocontrolled total synthesis of resiniferatoxin via an intramol. oxidopyrylium cycloaddn.)

RN 57444-62-9 CAPLUS

CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN

AB For the 1st time a normal-phase HPLC method using photodiode-array detection is described for the anal. and purification of phorbol esters. The use of the method is demonstrated with examples of 10 different tigliane and daphnane esters (TPA, DOPP, DOPPA, Sap A, Sap B. Sap C, Sap D, Thy A, Ro and Rx). Both anal. and semi-preparative techniques were developed. The method has been used in the final purification of DOPP and Rx from plant exts. The method can be employed in the areas of phytochem., biochem. and pharmacol./toxicol., where small samples of the toxic materials are required for research.

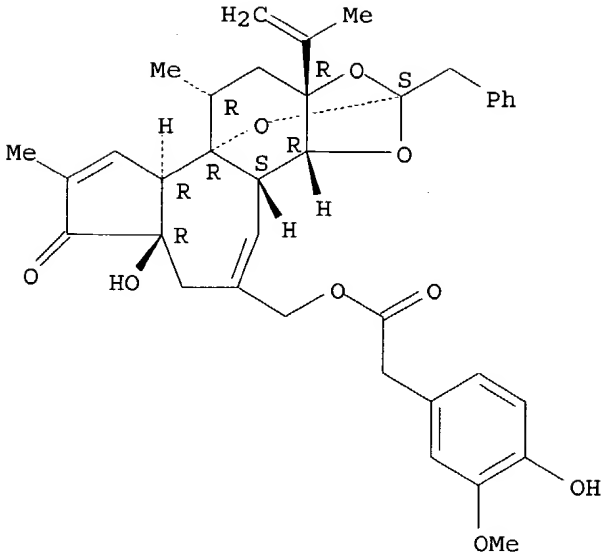
ACCESSION NUMBER: 1996:723646 CAPLUS
DOCUMENT NUMBER: 126:44504
TITLE: Analysis and purification of phorbol esters using normal phase HPLC and photodiode-array detection
AUTHOR(S): Dimitrijevic, Sasa M.; Humer, Ursula; Shehadeh, Mayadah; Ryves, W. Jonathan; Hassan, Nahed M.; Evans, Fred J.
CORPORATE SOURCE: Dep. Pharmacognosy, Univ. London, WC1N 1AX, UK
SOURCE: Journal of Pharmaceutical and Biomedical Analysis (1996), 15(3), 393-401
CODEN: JPBADA; ISSN: 0731-7085
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **57444-62-9P**, Resiniferatoxin
RL: ANT (Analyte); PRP (Properties); PUR (Purification or recovery); ANST (Analytical study); **PREP (Preparation)**
(anal. and purification of phorbol esters using normal phase HPLC and photodiode-array detection)

RN 57444-62-9 CAPLUS

CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 15 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
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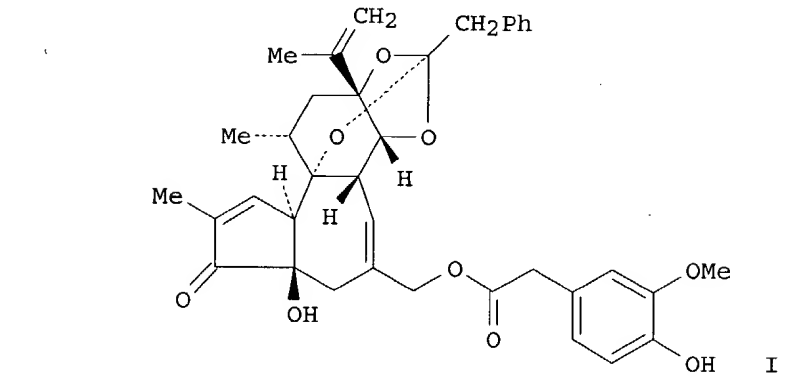

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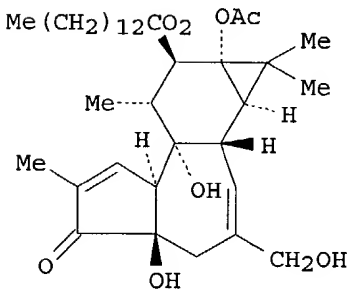
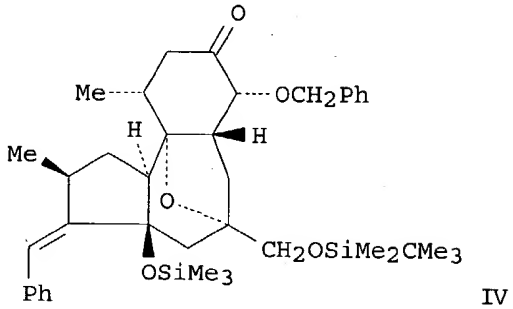


II



IV

AB A symposia report on resiniferatoxin (I), a structurally unique daphnane-type diterpene, which was identified in the latex of three species of Euphorbia on the basis of its extraordinary irritant activity. Structurally, I is similar to phorbol-related diterpenes. Unlike the most active phorbol myristate acetate (II), however, I is not a tumor promoter and does not compete for the phorbol ester binding site on kinase C. I also displays structural similarity to capsaicin, (E)-4-HO-3-

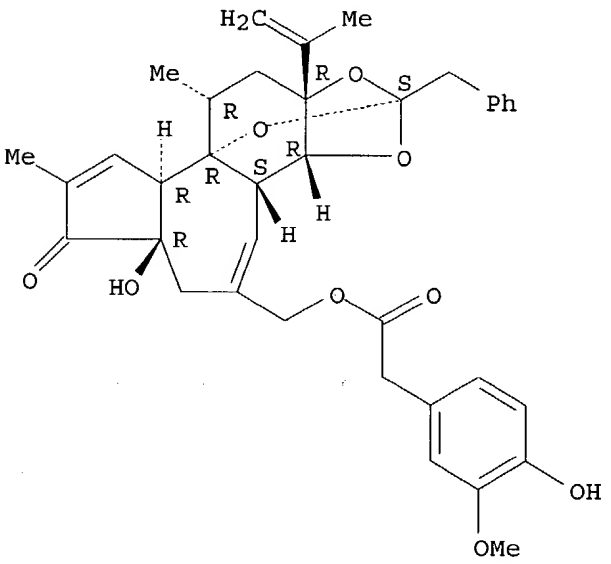
MeOC6H4CH2NHCO(CH2)4CH:CHCHMe (III), the major active constituent of common red pepper showing potent irritant and nociceptive properties. Indeed, I acts as a superpotent III analog and displays 103-104 times greater potency than III for many of these biol. responses. Herein a convergent and enantioselective synthesis of tricycle IV, a general precursor to the daphnanes, and the first total synthesis of I in 23 steps from IV is detailed.

ACCESSION NUMBER: 1996:703742 CAPLUS
DOCUMENT NUMBER: 126:31505
TITLE: Enantioselective total synthesis of resiniferatoxin: First synthesis of a daphnane diterpene
AUTHOR(S): Nakahira, Hiroyuki; Ueno, Yoshihide; Tamura, Norikazu
CORPORATE SOURCE: Sumitomo Pharmaceuticals, Ltd., Japan
SOURCE: Tennen Yuki Kagobutsu Toronkai Koen Yoshishu (1996), 38th, 571-576
CODEN: TYKYDS
PUBLISHER: Nippon Kagakkai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

IT **57444-62-9P**, (+)-Resiniferatoxin
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(enantioselective total synthesis of resiniferatoxin and the key intermediate to daphnane diterpenes)

RN 57444-62-9 CAPLUS
CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 16 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
AB Structure-activity relationships in analogs of the irritant natural product capsaicin have previously been rationalized by subdivision of the mol. into three structural regions (A, B, and C). The hypothesis that resiniferatoxin (RTX), which is a high-potency ligand for the same receptor and which has superficial structural similarities with capsaicin, could be analogously subdivided has been investigated. The effects of making parallel changes in the two structural series have been studied in a cellular functional assay which is predictive of analgesic activity. Parallel structural changes in the two series lead to markedly different

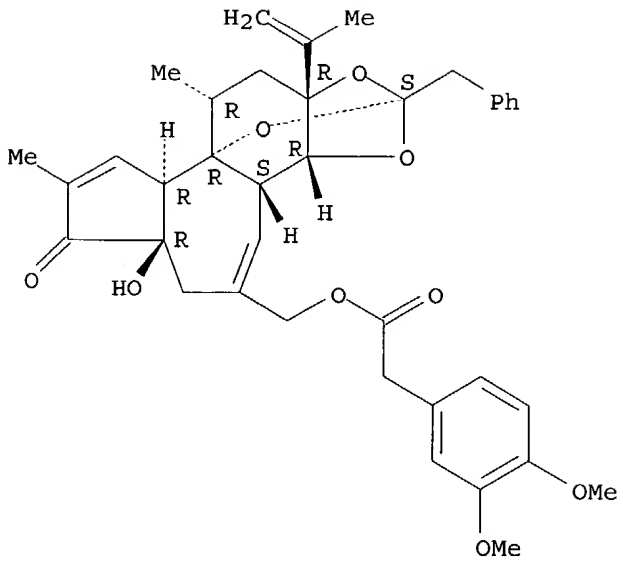
consequences on biol. activity; the 3- and 4-position aryl substituents (corresponding to the capsaicin 'A-region') which are strictly required for activity in capsaicin analogs are not important in RTX analogs. The homovanillyl C-20 ester group in RTX (corresponding to the capsaicin 'B-region') is more potent than the corresponding amide, in contrast to the capsaicin analogs. Structural variations to the diterpene moiety suggest that the functionalized 5-membered diterpene ring of RTX is an important structural determinant for high potency. Modeling studies indicate that the 3D position of the α-hydroxy ketone moiety in the 5-membered ring is markedly different in the phorbol (inactive) analogs and RTX (active) series. This difference appears to be due to the influence of the strained ortho ester group in RTX, which acts as a local conformational constraint. The reduced activity of an analog substituted in this region and the inactivity of a simplified analog in which this unit is entirely removed support this conclusion.

ACCESSION NUMBER: 1996:383038 CAPLUS
DOCUMENT NUMBER: 125:143055
TITLE: Similarities and Differences in the Structure-Activity Relationships of Capsaicin and Resiniferatoxin Analogs
AUTHOR(S): Walpole, Christopher S. J.; Bevan, Stuart; Bloomfield, Graham; Breckenridge, Robin; James, Iain F.; Ritchie, Timothy; Szallasi, Arpad; Winter, Janet; Wrigglesworth, Roger
CORPORATE SOURCE: Sandoz Institute for Medical Research, London, WC1E 6BN, UK
SOURCE: Journal of Medicinal Chemistry (1996), 39(15), 2939-2952
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **83117-38-8P 179469-37-5P 179469-43-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**
(preparation and structure-activity relationships of capsaicin and resiniferatoxin analogs)

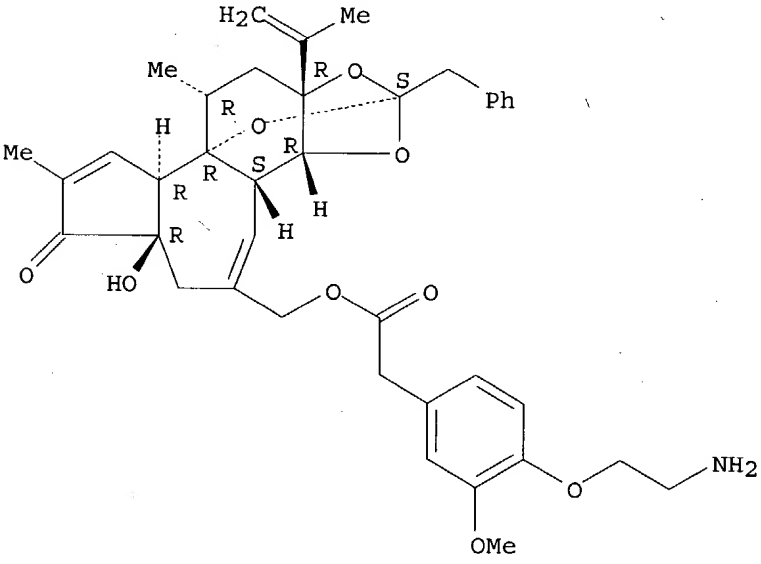
RN 83117-38-8 CAPLUS
CN Benzeneacetic acid, 3,4-dimethoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



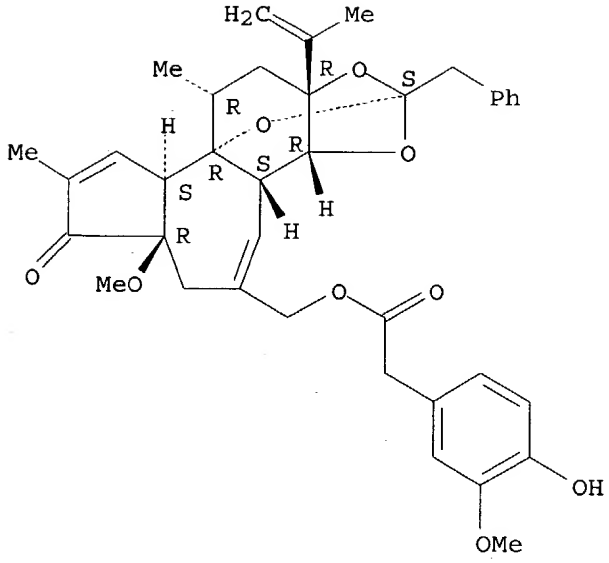
RN 179469-37-5 CAPLUS
CN Benzeneacetic acid, 4-(2-aminoethoxy)-3-methoxy-, [3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester, [2S-(2α,3aβ,3bβ,6aβ,9aα,9bα,10.alpha.,11aβ)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 179469-43-3 CAPLUS
CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [3a,3b,6,6a,9a,10,11,11a-octahydro-6a-methoxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester, [2S-(2α,3aβ,3bβ,6aβ,9aα,9bα,10.alpha.,11aβ)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



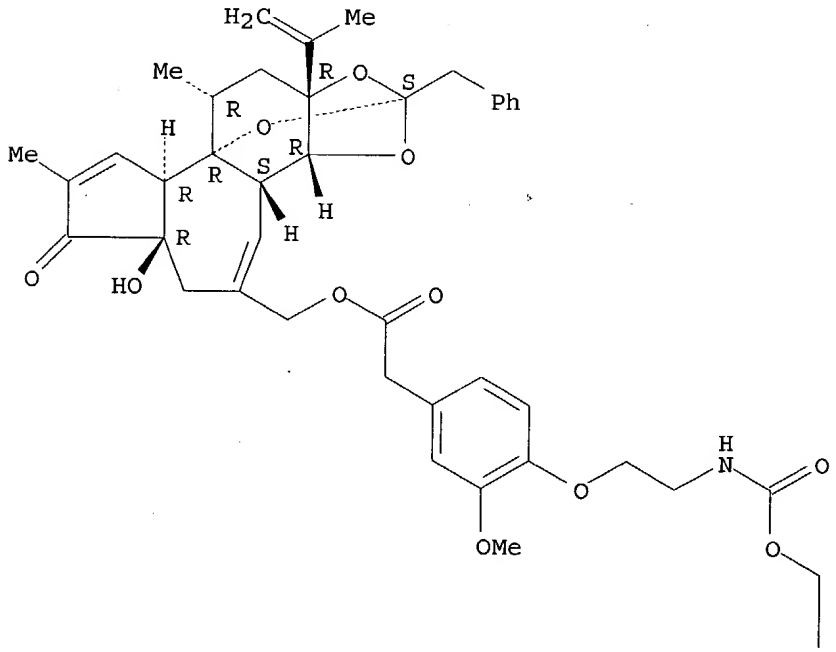
IT **179469-52-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and structure-activity relationships of capsaicin and resiniferatoxin analogs)

RN 179469-52-4 CAPLUS

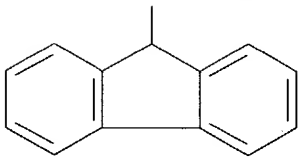
CN Benzeneacetic acid, 4-[2-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]ethoxy]-3-methoxy-, [3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester, [2S-(2α,3aβ,3bβ,6a.beta.,9aα,9bα,10α,11aβ)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



L4 ANSWER 17 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN

AB Bioactivity-guided fractionation of the latex of Euphorbia poisonii Pax. (Euphorbiaceae) led to the isolation and characterization of a new tigliane diterpene, 12-deoxyphorbol 13-(9,10-methylene)undecanoate, together with five known diterpenes. When evaluated for cytotoxicity in a panel of six human solid tumor cell lines, the diterpene esters were selectively cytotoxic for the human kidney carcinoma (A-498) cell line with potencies for 2 and 3 exceeding that of adriamycin by ten thousand times. Details of the isolations, structural analyses, and cytotoxic activities are described.

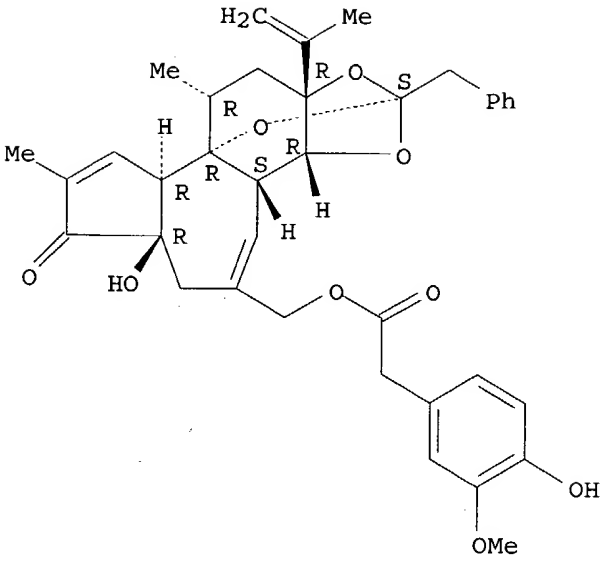
ACCESSION NUMBER: 1996:73864 CAPLUS
DOCUMENT NUMBER: 124:112413
TITLE: Selectively Cytotoxic Diterpenes from Euphorbia poisonii
AUTHOR(S): Fatope, Majekodunmi O.; Zeng, Lu; Ohayaga, Joseph E.; Shi, Guoen; McLaughlin, Jerry L.
CORPORATE SOURCE: School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, IN, 47907, USA
SOURCE: Journal of Medicinal Chemistry (1996), 39(4), 1005-8
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **57444-62-9P**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); **PREP (Preparation)**
(selectively cytotoxic diterpenes from Euphorbia poisonii)

RN 57444-62-9 CAPLUS

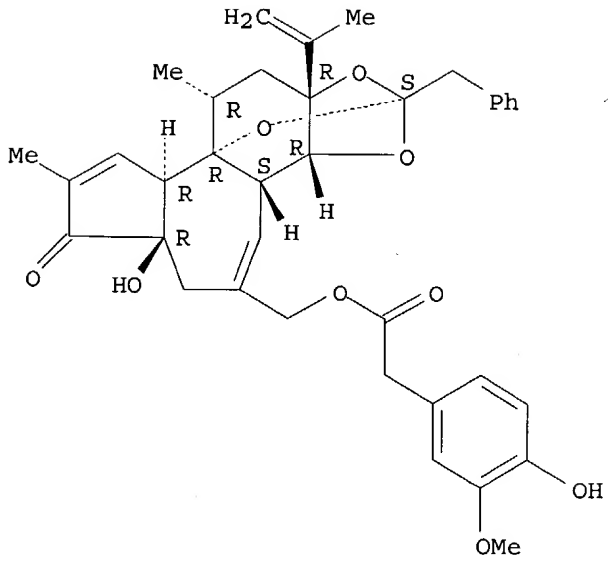
CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 18 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
AB Unavailable
ACCESSION NUMBER: 1996:15810 CAPLUS
DOCUMENT NUMBER: 124:117630
TITLE: The first asymmetric synthesis of the complete daphnane skeleton
AUTHOR(S): Jesudason, Cynthia Darshini
CORPORATE SOURCE: Stanford Univ., Stanford, CA, USA
SOURCE: (1995) 295 pp. Avail.: Univ. Microfilms Int., Order No. DA9535607
From: Diss. Abstr. Int., B 1995, 56(6), 3201
DOCUMENT TYPE: Dissertation
LANGUAGE: English
IT **57444-62-9P**, Resiniferatoxin
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(asym. synthesis of the complete daphnane skeleton)
RN 57444-62-9 CAPLUS
CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 19 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN

AB The title compound was prepared from resiniferol by oxidation to the aldehyde, reduction with NaB3H4, and esterification. This compound will be of use in the elucidation of the binding characteristics of resiniferatoxin to its biochem. receptor site(s).

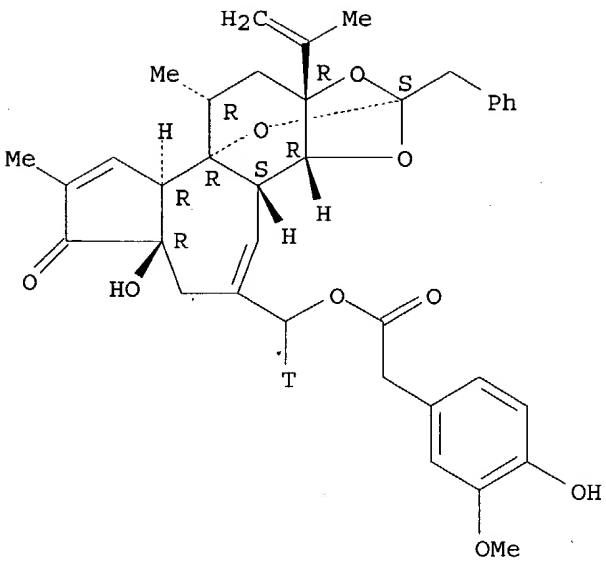
ACCESSION NUMBER: 1995:175129 CAPLUS
DOCUMENT NUMBER: 122:160980
TITLE: semi-synthesis of C20 3H-resiniferatoxin
AUTHOR(S): Gordge, Phil C.; Darcy, Patricia; Evans, A. Tudor; Ryves, W. Jonathan; Evans, Fred J.; Hassan, Nahed M.
CORPORATE SOURCE: Department of Pharmacognosy, School of Pharmacy, London, WC1N 1AX, UK
SOURCE: Phytotherapy Research (1994), 8(6), 362-4
CODEN: PHYREH; ISSN: 0951-418X
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **161057-64-3P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of 20-3H-resiniferatoxin)

RN 161057-64-3 CAPLUS

CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl-t ester, [2S-(2α,3aβ,3bβ,6aβ,9aα,9bα,10.alp ha.,11aβ)]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 20 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN
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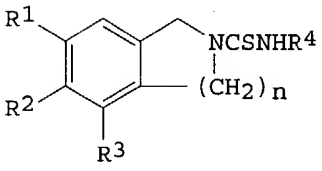


I

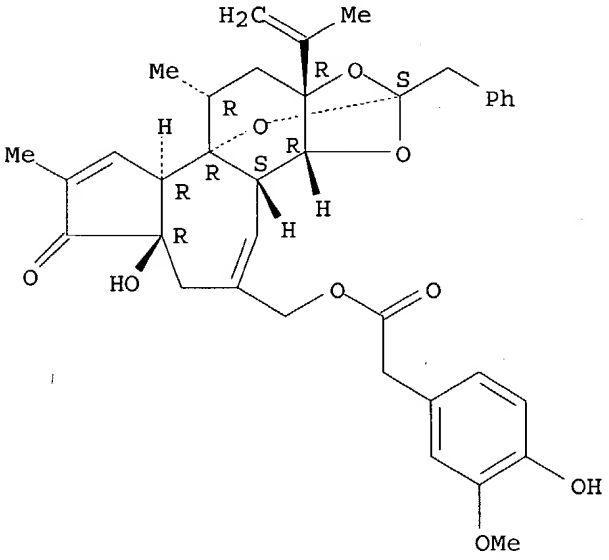
AB Capsaicin and resiniferatoxin are natural products which act specifically on a subset of primary afferent sensory neurons to open a novel cation-selective ion channel in the plasma membrane. Conformationally constrained analogs I [R1 = OH, OMe, H; R2 = OH, OMe; R3 = H, OH; R4 = octyl, 4-ClC6H4CH2CH2; n = 1-3] of these mols. were prepared The resulting compds. provided agonists of comparable potency to unconstrained analogs as well as a moderately potent antagonist, capsazepine (I, R1 = R2 = OH, R3 = H, R4 = 4-ClC6H4CH2CH2, n = 3). This compound is the first competitive antagonist of capsaicin and resiniferatoxin to be described and is active in various systems, in vitro and in vivo.

ACCESSION NUMBER: 1994:483028 CAPLUS
DOCUMENT NUMBER: 121:83028
TITLE: The Discovery of Capsazepine, the First Competitive Antagonist of the Sensory Neuron Excitants Capsaicin and Resiniferatoxin
AUTHOR(S): Walpole, Christopher S. J.; Bevan, Stuart; Bovermann, Guenter; Boelsterli, Johann J.; Breckenridge, Robin; Davies, John W.; Hughes, Glyn A.; James, Iain; Oberer, Lukas; et al.
CORPORATE SOURCE: Sandoz Institute for Medical Research, London, WC1E 6BN, UK
SOURCE: Journal of Medicinal Chemistry (1994), 37(13), 1942-54
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **57444-62-9DP**, Resiniferatoxin, conformationally restricted analogs
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation and agonist activity of)

RN 57444-62-9 CAPLUS
CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11a R)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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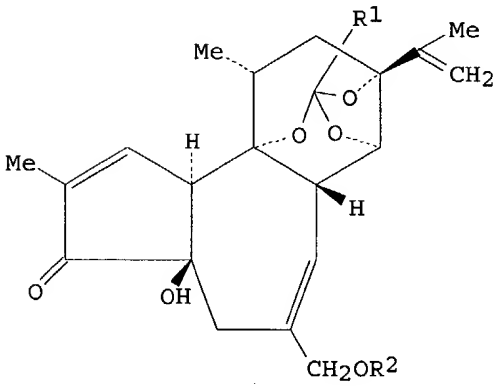


I

AB The preparation of the daphnane prototype polyfunctional diterpene resiniferonol from resiniferatoxin (I; R1 = CH2Ph, R2 = COCH2C6H3OMe-3-OH-4) contained in latex from Euphoriba unispina or E. poisonii was modified to convert in an 'early' fraction of the acetone extract the extremely irritant I to the much less irritant 9,13,14-ortho(phenylacetate) I (R1 = CH2Ph, R2 = H) by transesterification. I (R1 = CH2Ph, R2 = H) was obtained in good yields and can be handled conveniently to prepare resiniferonol as reported previously. By esterification of resiniferonol with homologous straight chain aliphatic acids from C2 to C18 resiniferonol-14,20-diacylates were prepared Treatment of the diacylates with perchloric acid/methanol yielded by intramol. formation of the orthoester function the corresponding

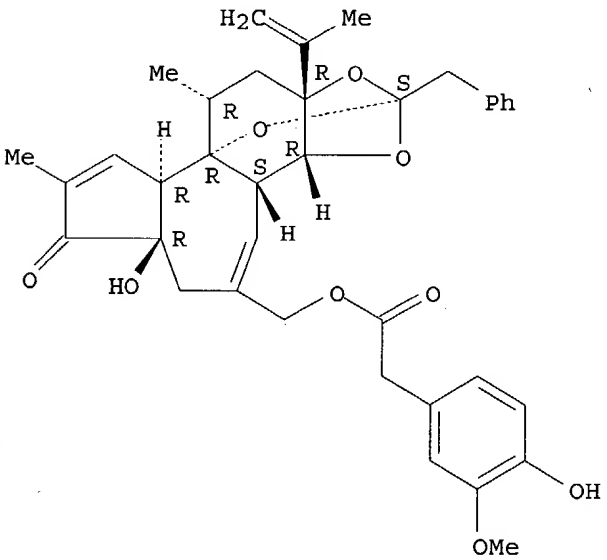
9,13,14-orthoester-20-acylates. They were cleaved selectively by base catalyzed transesterification to obtain the resiniferonol-9,13,14-orthoacetate (I; R1 = Me, R2 = H), -hexanoate [I; R1 = (CH2)4Me, R2 = H], -decanoate [I; R1 = (CH2)8Me, R2 = H], -tetradecanoate [I; R1 = (CH2)12Me, R2 = H] and -octadecanoate [I; R1 = (CH2)16Me, R2 = H]. On the mouse ear, unexpectedly they exhibit only weak irritant activity and on the mouse back skin practically no tumor promoting activity.

ACCESSION NUMBER: 1993:449681 CAPLUS
DOCUMENT NUMBER: 119:49681
TITLE: On the chemistry of resiniferonol. I. Preparation of resiniferonol, synthesis of homologous aliphatic resiniferonol-9,13,14-orthoesters and some of their bioactivities
AUTHOR(S): Adolf, W.; Hecker, E.
CORPORATE SOURCE: Dtsch. Krebsforschungszent., Heidelberg, D-W-6900, Germany
SOURCE: Zeitschrift fuer Naturforschung, B: Chemical Sciences (1993), 48(3), 364-8
CODEN: ZNBSEN; ISSN: 0932-0776
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 119:49681

IT **57444-62-9P**
RL: RCT (Reactant); **PREP (Preparation)**; RACT (Reactant or reagent)
(isolation and deacylation of)

RN 57444-62-9 CAPLUS
CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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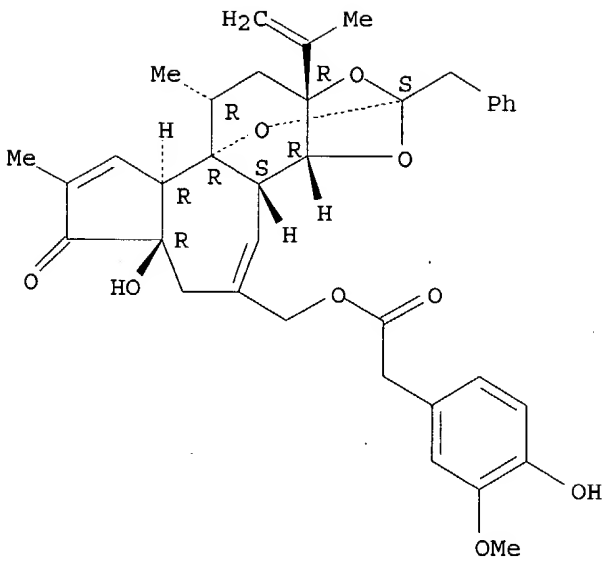
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Structurally simplified analogs of the daphnane diterpene resiniferatoxin , possessing the unusual 2,9,10-trioxatricyclo[4.3.1.03.8]decane system were synthesized stereoselectively from 1,3-cyclohexadiene: functionalization of the diene afforded the anti-epoxide, 1,4-di-O-benzyl-t-2,t-3-epoxycyclohexane-r-1,c-4-diol (I), whose ring-opening was examined using various organometallic reagents; organoaluminum species were found to be the most efficient to effect this reaction. When trimethylsilyl (in place of benzyl) ethers were used to protect the diol, selective deprotection of 1,4-di-O-trimethylsilyl-2-O-(p-tolylsulfonyl)-c-3-[3-(tert-butyldiphenylsilyloxy)prop-1-ynyl]cyclohexane-r-1,t-2,c-4-triol II (Ts = tosyl) was achieved using citric acid in methanol - the equatorially disposed trimethylsilyl ether was found to be more easily cleaved than the axially oriented one. Formation of the tricyclic orthoester was achieved by the generation of a dioxolenium ion from 1-O-phenylacetyl-2-O-(p-tolylsulfonyl)-c-3-[3-(tert-butyldiphenylsilyloxy)prop-1-ynyl]cyclohexane-r-1,t-2,c-4-triol (III), by heating in 2,4,6-trimethylpyridine, with in situ intramol. trapping by the suitably oriented hydroxy group to give 1-benzyl-7-(3-tert-butyldiphenylsilyoxyprop-1-ynyl)-2,9,10-trioxatricyclo[4.3.1.03.8]decane (IV).

ACCESSION NUMBER: 1992:490529 CAPLUS
DOCUMENT NUMBER: 117:90529
TITLE: Synthesis of 2,9,10-trioxatricyclo[4.3.1.03.8]decane analogs of resiniferatoxin
AUTHOR(S): Bloomfield, Graham C.; Ritchie, Timothy J.; Wrigglesworth, Roger
CORPORATE SOURCE: Sandoz Inst. Med. Res., London, WC1E 6BN, UK
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1992), (10), 1229-36
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **57444-62-9P**, Resiniferatoxin
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of trioxatricyclodecane analog of)
RN 57444-62-9 CAPLUS
CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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AB Radiolabeled and fluorescent-substance-labeled derivs. of resiniferatoxin (I) (a naturally occurring ultrapotent capsaicin analog) and its congeners are disclosed. The labeled compds. of the invention are useful, e.g. in demonstrating and characterizing specific capsaicin receptors. Thus, 3H-I (II) was prepared from 3H-homovanillic acid and resiniferonol ortheophenylacetate. Binding of II to membrane prepns. of rat dorsal not ganglia was characterized by Scatchard anal. Capsaicin inhibited specific binding of II to a pig dorsal root ganglion membrane preparation; piperadine and zingerone did not inhibit or did so more weakly. II binding was not inhibited by e.g. resiniferonol 9,13,14-orthophenylacetate or phorbol 12,13-dibutyrate. A tablet formulation of II is given.

ACCESSION NUMBER: 1991:627805 CAPLUS
DOCUMENT NUMBER: 115:227805
TITLE: Labeled resiniferatoxin, its compositions, and its use, especially in capsaicin receptor characterization
INVENTOR(S): Blumberg, Peter M.; Szallasi, Arpad; Szallasi, Zoltan
PATENT ASSIGNEE(S): National Institutes of Health, USA
SOURCE: U. S. Pat. Appl., 48 pp. Avail. NTIS Order No. PAT-APPL-7-546 141.
CODEN: XAXXAV
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 546141	A0	19910415	US 1990-546141	19900629
US 5232684	A	19930803		

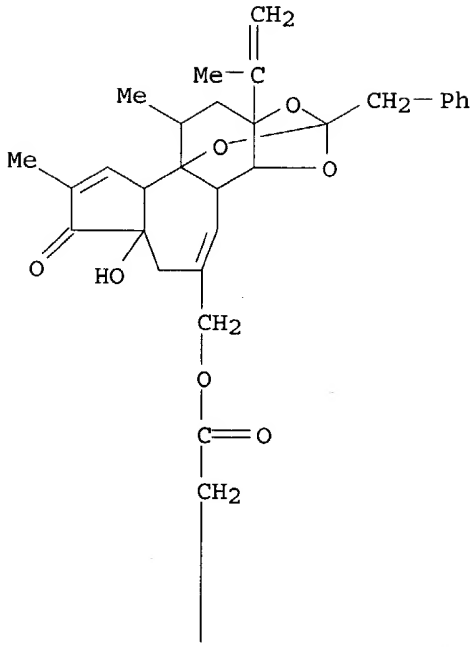
PRIORITY APPLN. INFO.: US 1990-546141 19900629
OTHER SOURCE(S): MARPAT 115:227805

IT **136849-17-7P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of, for capsaicin receptor characterization)

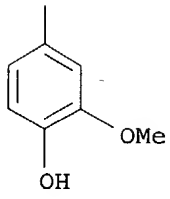
RN 136849-17-7 CAPLUS

CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester, labeled with tritium (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



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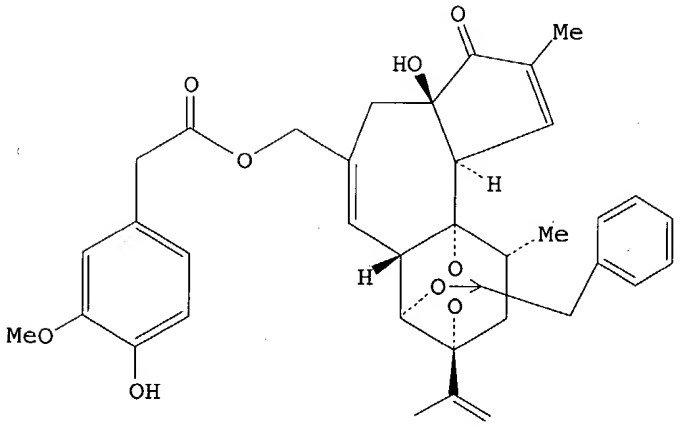


I

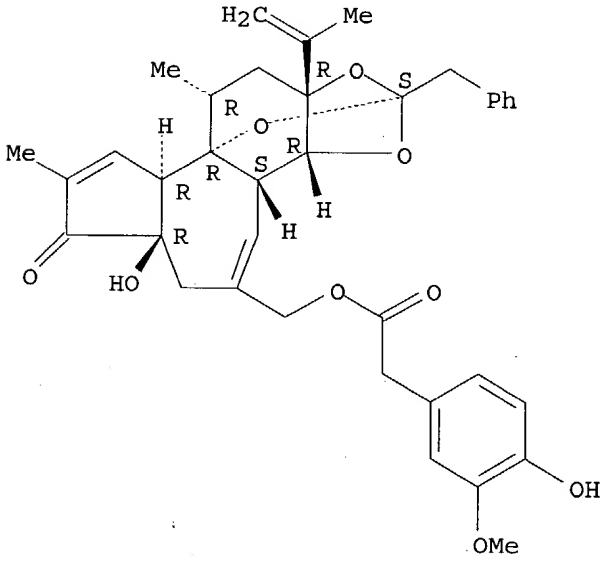
AB Structurally simplified analogs of the diterpene resinferatoxin (I) possessing a 2,9,10-trioxatricyclo[4.3.1.03,8]decane system were synthesized stereoselectively from cyclohexa-1,3-diene.

ACCESSION NUMBER: 1991:229181 CAPLUS
DOCUMENT NUMBER: 114:229181
TITLE: The stereoselective synthesis of 2,9,10-trioxatricyclo[4.3.1.03,8]decane analogs of resiniferatoxin
AUTHOR(S): Bloomfield, Graham C.; Wrigglesworth, Roger; Ritchie, Timothy J.
CORPORATE SOURCE: Sandoz Inst. Med. Res., London, WC1E 6BN, UK
SOURCE: Journal of the Chemical Society, Chemical Communications (1991), (4), 215-17
CODEN: JCCCAT; ISSN: 0022-4936
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:229181

IT **57444-62-9DP**, Resiniferatoxin, analogs
RL: RCT (Reactant); **PREP (Preparation)**; RACT (Reactant or reagent)
(stereoselective synthesis of)

RN 57444-62-9 CAPLUS
CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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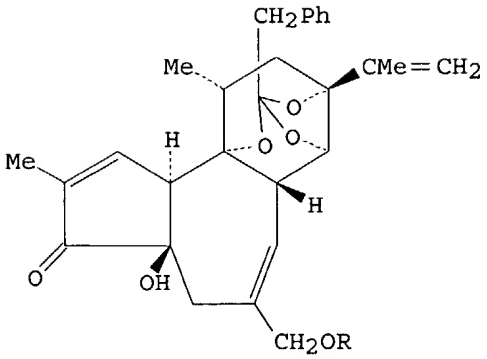
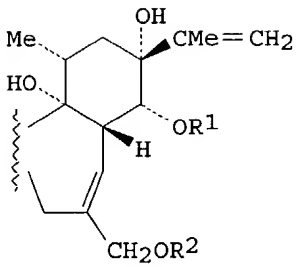


I



II

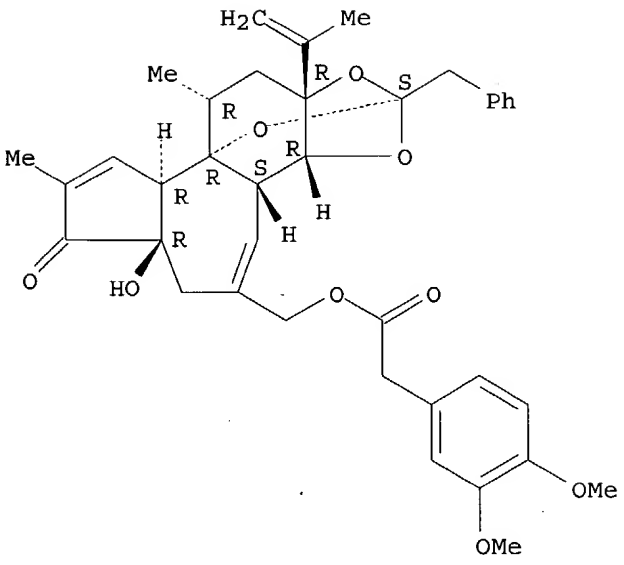
AB The structure of resiniferatoxin was revised to I [R = 4,6-HO(MeO)C6H3CH2CO] as a result of synthesis. Esters I [R = 3,4- and 3,5-(MeO)2C6H3CH2CO, PhCH2CO, Bz, Me(CH2)4CO, Ac] and II [R1 = R2 = Ac, Me(CH2)2CO] were prepared and their irritant activity and that of resiniferonol (II, R1 = R2 = H) were correlated with the acid moiety and the position of the arom ring.

ACCESSION NUMBER: 1982:545052 CAPLUS
DOCUMENT NUMBER: 97:145052
TITLE: Structure-activity relations of polyfunctional diterpenes of the daphnane type. I. Revised structure for resiniferatoxin and structure-activity relations of resiniferonol and some of its esters
AUTHOR(S): Adolf, W.; Sorg, B.; Hergenhahn, M.; Hecker, E.
CORPORATE SOURCE: Inst. Biochem., Dtsch. Krebsforschungszent., Heidelberg, 6900, Fed. Rep. Ger.
SOURCE: Journal of Natural Products (1982), 45(3), 347-54
CODEN: JNPRDF; ISSN: 0163-3864
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **83117-38-8P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation and irritant activity of)

RN 83117-38-8 CAPLUS
CN Benzeneacetic acid, 3,4-dimethoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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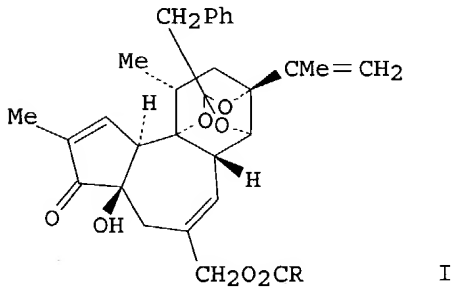
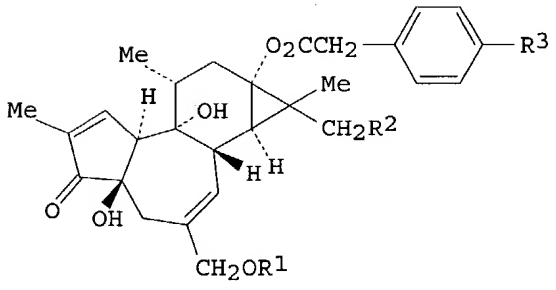


I



II

AB Resiniferonol esters I [R = CH2C6H3(OH)OMe-3,5; CH2C6H4OH-p; Me], 12-deoxy-16-hydroxyphorbol esters II (R1 = H, Ac, R2 = O2CCHMeEt, R3 = H), and the deoxyphorbol esters II (R1 = Ac, R2 = H, R3 = OH; R1 = Ac, R2 = H, R3 = OAc; R1 = Ac, R2 = R3 = H; R1 = R2 = R3 = H) were isolated from E. poissonii and their structures determined on the basis of their IR, UV, NMR, and mass spectra and by chemical correlations. Their irritant potency was also evaluated.

ACCESSION NUMBER: 1980:111182 CAPLUS
DOCUMENT NUMBER: 92:111182
TITLE: The succulent euphorbias of Nigeria. III. Structure and potency of the aromatic ester diterpenes of Euphorbia poissonii Pax

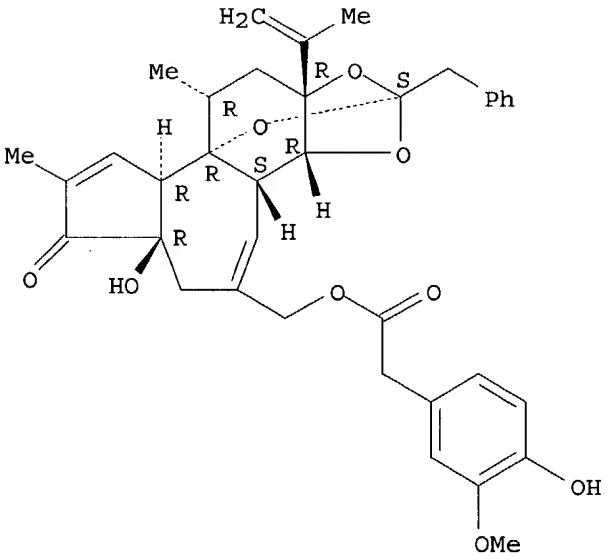
AUTHOR(S): Evans, Fred J.; Schmidt, Richard J.
CORPORATE SOURCE: Sch. Pharm., Univ. London, London, WC1N 1AX, UK
SOURCE: Acta Pharmacologica et Toxicologica (1979), 45(3), 181-91
CODEN: APTOA6; ISSN: 0001-6683
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **57444-62-9P**
RL: **PREP (Preparation)**
(from Euphorbia poissonii, mol. structure determination and irritant potency of)

RN 57444-62-9 CAPLUS

CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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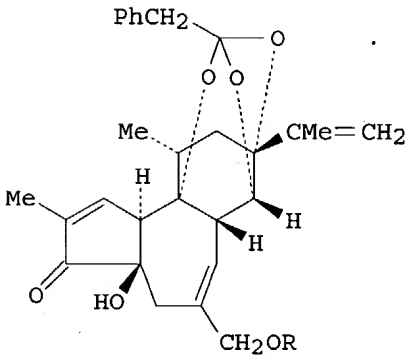


I

AB A series of esters (I) were produced by partial synthesis from 9,13,14-orthophenylacetylresiniferonol (I, R = H)(II) [57852-42-3]. I

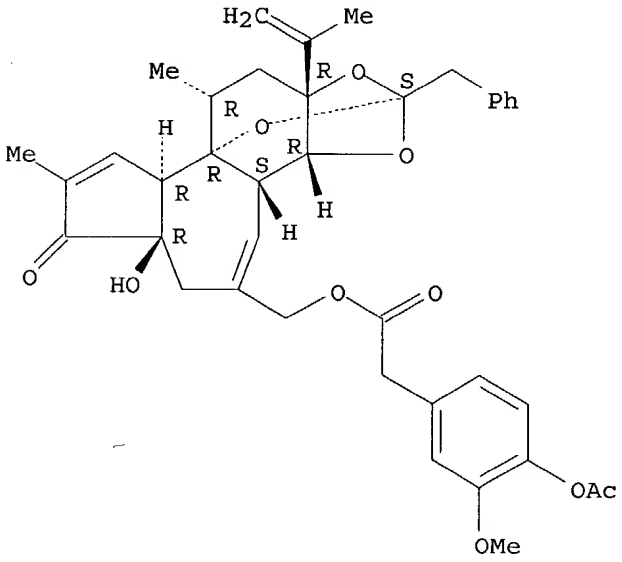
were tested for irritant effects by means of a mouse ear assay. All I, including II, produced short-term inflammation of mice ears 1-2 h and the effects did not persist for more than 24 h. This was in contrast to esters of structurally related tigliane diterpenes which produce a longer-term effect on mice ears. Highly potent irritants which were synthesized exhibited irritant doses (0.0012-0.00021 nmol). The meta or para positions of the phenylacetate moiety of I were substituted with electroneg. groups for maximum activity. I (R = substituted phenylpropionate) were not irritants in the test.

ACCESSION NUMBER: 1979:552170 CAPLUS
DOCUMENT NUMBER: 91:152170
TITLE: Investigations into the skin-irritant properties of resiniferonol ortho esters
AUTHOR(S): Schmidt, Richard J.; Evans, Fred J.
CORPORATE SOURCE: Sch. Pharm., Univ. London, London, WC1N 1AX, UK
SOURCE: Inflammation (New York, NY, United States) (1979), 3(3), 273-80
CODEN: INFLD4; ISSN: 0360-3997
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **71407-32-4P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of, skin irritation from)

RN 71407-32-4 CAPLUS
CN Benzeneacetic acid, 4-(acetyloxy)-3-methoxy-, [3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester, [2S-(2α,3aβ,3bβ,6aβ,9aα,9bα,10.alpha.,11aβ)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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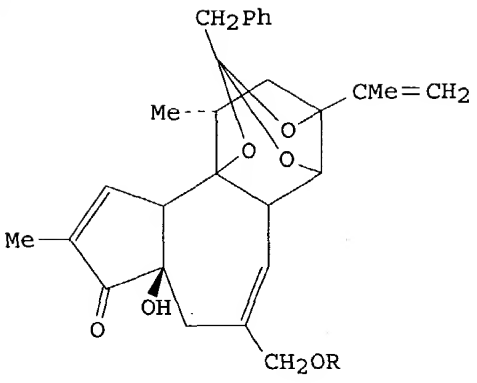


I

AB Diterpenes I (R = COCH2C6H3MeOH-3,5, COCH2C6H4OH-p, H, Ac) were isolated from the latex of E. poissoni and their structures determined in the basis of their ir, uv, NMR, and mass spectra.

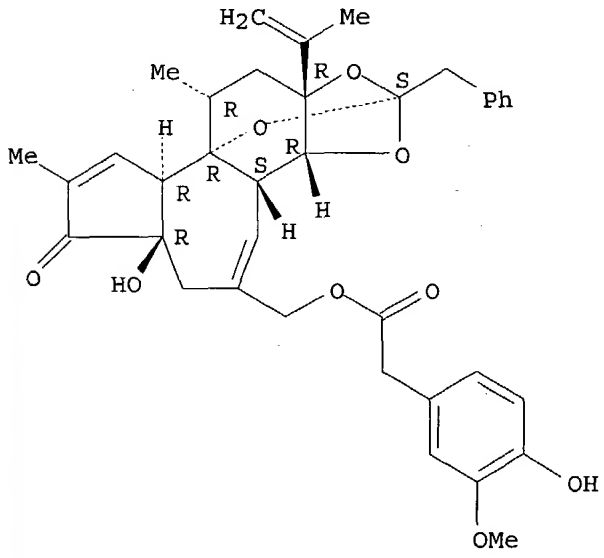
ACCESSION NUMBER: 1976:421638 CAPLUS
DOCUMENT NUMBER: 85:21638
TITLE: Two new toxins from the latex of Euphorbia poisonii
AUTHOR(S): Evans, Fred J.; Schmidt, Richard J.
CORPORATE SOURCE: Sch. Pharm., Univ. London, London, UK
SOURCE: Phytochemistry (Elsevier) (1976), 15(2), 333-5
CODEN: PYTCAS; ISSN: 0031-9422
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **57444-62-9P**
RL: **PREP (Preparation)**
(from latex of Euphorbia poisonii)

RN 57444-62-9 CAPLUS

CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 29 OF 29 CAPLUS COPYRIGHT 2004 ACS on STN

GI For diagram(s), see printed CA Issue.

AB The nonirritant compds. I and II, and irritant factors RL14 (III), resiniferatoxin (IV), and proresiniferatoxin (V) were isolated from the latex of E. resinifera. IV was also obtained from E. unispina. The structures of I-V were determined from chemical and spectral data.

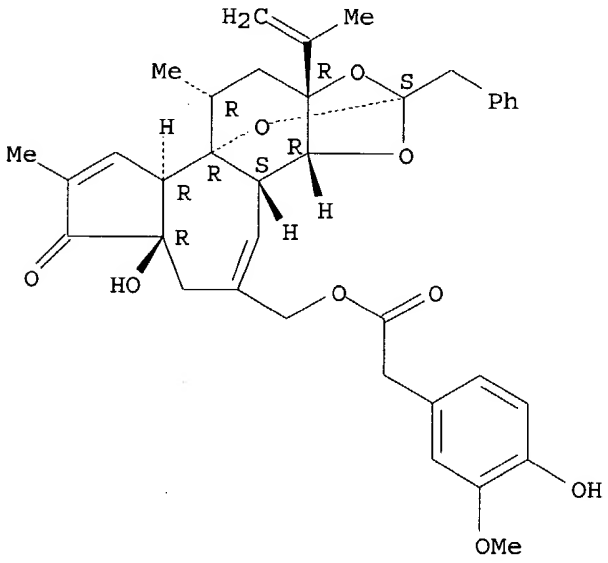
ACCESSION NUMBER: 1975:497619 CAPLUS
DOCUMENT NUMBER: 83:97619
TITLE: Resiniferatoxin and other esters of novel polyfunctional diterpenes from Euphorbia resinifera and unispina
AUTHOR(S): Hergenhahn, M.; Adolf, W.; Hecker, E.
CORPORATE SOURCE: Inst. Biochem., Dtsch. Krebsforsch., Heidelberg, Fed. Rep. Ger.
SOURCE: Tetrahedron Letters (1975), (19-20), 1595-8
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **57444-62-9P**
RL: **PREP (Preparation)**
(from Euphorbia resinifera, structure of)

RN 57444-62-9 CAPLUS

CN Benzeneacetic acid, 4-hydroxy-3-methoxy-, [(2S,3aR,3bS,6aR,9aR,9bR,10R,11aR)-3a,3b,6,6a,9a,10,11,11a-octahydro-6a-hydroxy-8,10-dimethyl-11a-(1-methylethenyl)-7-oxo-2-(phenylmethyl)-7H-2,9b-epoxyazuleno[5,4-e]-1,3-benzodioxol-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> s l4 and iodine
124689 IODINE
194 IODINES
124763 IODINE
(IODINE OR IODINES)
L5 0 L4 AND IODINE

=> s l4 and iodination
15465 IODINATION
101 IODINATIONS
15492 IODINATION
(IODINATION OR IODINATIONS)

L6 1 L4 AND IODINATION

=> d l6

L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:251346 CAPLUS
DN 137:125294
TI Synthesis and in vitro evaluation of a novel iodinated resiniferatoxin derivative that is an agonist at the human vanilloid VR1 receptor
AU McDonnell, Mark E.; Zhang, Sui-Po; Dubin, Adrienne E.; Dax, Scott L.
CS Johnson & Johnson Pharmaceutical Research and Development, Spring House, PA, 19477, USA
SO Bioorganic & Medicinal Chemistry Letters (2002), 12(8), 1189-1192
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 137:125294
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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